ISSN 1331-7210

Engineering Power

BULLETIN OF THE CROATIAN ACADEMY OF ENGINEERING Vol. 12(2) 2017

EDITOR-IN-CHIEF'S WORD

Dear Readers,

It is with great pride and joy that we are able to present you, shortly after this year's first issue of the ***„Engineering Power“***, the double issue of our Academy's Bulletin in Croatian and in English, ***„Tehničke znanosti“*** Vol. 21(1) 2017 / ***„Engineering Power“*** Vol. 12(2) 2017.

This issue is prepared in co-operation of the Guest-Editor Mario Cifrek, Associate Member of the Academy, with his colleagues and co-workers from the Faculty of Electrical Engineering and Computing in Zagreb and the University Hospital Centre Zagreb. The issue is dedicated to selected current research projects in neurophysiology, which address brain electrical signals i.e. their measurement, processing, analysis, and application.

As a scientific organisation dedicated to promotion and popularisation of technological and biotechnological sciences, facilitating continuous cooperation of our most prominent scientists as well as strengthening the public awareness of the importance of technological and biotechnological sciences, our Academy consistently and tirelessly strives to bring to our readers from all fields and professions the most important and valuable insights into our members' activities, and into the state of individual domains in technological and biotechnological sciences.

Editor-in-Chief
Vladimir Andročec, President of the Croatian Academy of Engineering

EDITOR'S WORD

Mutual permeation of engineering sciences and contemporary medical practice is one of the best examples of the necessity of multi-disciplinary approach in present-day science. From computer modelling and numerical simulations of physical and chemical processes within the biological systems, and utilisation of instrumentarium based on more and more sophisticated technological solutions for diagnostical purposes, to intelligent orthopedic apparatuses and smart prosthetics *(„wearable robotics“)*, the application of advanced engineering solutions has been inevitable in almost all domains of the contemporary medicine.

The awareness of the necessity of such interconnection is reflected in the everyday activities of the Croatian Academy of Engineering, which closely co-operates with the Croatian Academy of Medical Sciences and clinical and research institutions within the frame of work on joint projects, the organisation of scientific conferences, and other socially important activities.

Having in mind all aforementioned, I am especially pleased to present you this issue of the ***„Engineering Power“***, which addresses a subject that interconnects the domains of engineering activities and medical practice in a particularly relevant manner. The Guest-Editor of this issue is Mario Cifrek, Associate Member of the Croatian Academy of Engineering in the Department of Systems and Cybernetics, and Full Professor at the Faculty of Electrical Engineering and Computing of the University of Zagreb.

Editor
Zdravko Terze, Vice-President of the Croatian Academy of Engineering

GUEST-EDITOR'S WORD

Brain electrical signals – measurement, processing, analysis, and applications

Biomedical engineering is an interdisciplinary field combining knowledge of engineering (electrical engineering, computer science, information and communication technology, physics, chemistry ...), biology and medicine. The development of medical science, health service organisation and health care at the turn of this century is closely and inseparably linked to the development of electronic, computer, information and communication technologies. Electrical equipment and accessories are an integral part of almost every medical examination/intervention, and computer and information and communication systems are now an inseparable part of everyday life.

Electroencephalography (EEG) is one of the basic neurophysiological methods of registration of the brain bioelectric activity. It was first mentioned in the thirties of the last century in the works of neuropsychiatrist Hans Berger. He was recording, using sensitive galvanometer, the first signals that belong to the alpha frequency range, according to today's classification. EEG as a diagnostic method begins routinely carried out with the first commercially available electroencephalograph in the fifties of the last century. Here we must point out Professor Ante Šantić who already in 1957, as an employee of the Institute of Electrical Engineering in Zagreb, designed and commercialised 12 channel electroencephalograph, the first in South-eastern/Central Europe. Upon arrival at the Faculty of Electrical Engineering, University of Zagreb, in 1972 he founded the Laboratory for Biomedical Electronics and starts lecturing on Biomedical Electronics, for which he wrote the textbook of the same name, and thus lays the foundation of biomedical engineering in Croatia. Technological progress made it possible to process electroencephalographic signals on the digital computer. Already in the beginning of the seventies, it was carried out on the PDP-8 computer by Prof. Stanko Tonković, PhD, Dipl Eng, an employee of the Faculty of Electrical Engineering in Zagreb, and Velimir Išgum, PhD, Dipl Eng, an employee of the Clinical Hospital Centre Zagreb. Velimir Išgum, PhD, continues his career in the Department of Neurology, University Hospital Centre Zagreb, where he participated in the founding of the Laboratory of evoked potentials. Additionally, he founded the Laboratory for Cognitive and Experimental Neurophysiology. Several papers listed thereafter represent a continuation of research that started in these laboratories.

Initiation and development of this inter- and multi-disciplinary area would be impossible without the support and active participation of medical doctors. This high quality and fruitful collaboration took place to this day, which is directly visible in the presented papers.

The following papers presented some of the current research projects in the field of neurophysiology that uses measurement, processing and analysis of the electroencephalographic signals. The first paper presents several modalities for brain-computer interface (BCI), very actively investigated area in the last years. The following paper deals with the application of invasive EEG monitoring in the surgical treatment of patients with pharmacoresistant epilepsy. The third document describes the use of the evoked potentials in the diagnosis of multiple sclerosis. The fourth paper describes the diagnostic value of vibration evoked potentials, while the fifth one deals with auditory evoked potentials with a focus on the used stimuli and paradigms.

Guest-Editor
Mario Cifrek, University of Zagreb, Faculty of Electrical Engineering and Computing Zagreb

Krešimir Friganović, Ana Branka Jerbić, Marko Medved, Tea Zavacki, Mario Cifrek

BRAIN-COMPUTER INTERFACES

University of Zagreb, Faculty of Electrical Engineering and Computing

INTRODUCTION

The goal of new researches and technologies is to help and ease everyday tasks in life. Today, we can find the assistive technologies in everyday use, from the voice commands in smartphones to the eye tracking technologies. Those technologies emerged from the human-computer interface field of research. Brain-computer interfaces (BCIs) are part of this wide field of research. The main goal of such systems is to connect human (subjects) intention and the physical interaction with environment to do some task. In such a way, difficulties with interaction for people who are unable to use current devices (disabled persons) or are completely unable to communicate with outside world (patients with locked-in syndrome) are bypassed. The applications of the BCI systems can be of great help if they are developed for the people with severe neuromuscular damage, occurred as the effect of spinal cord injury, amyotrophic lateral sclerosis, stroke, or cerebral paralysis [1]. Besidea these specific applications, the BCI systems can be used as part of the biofeedback systems, to record our psychophysical state (perhaps even unaware of it) and use the computer to train us or adapt the environment to suit our needs.

The BCI systems include measurement, analysis and evaluation of complex neurophysiological patterns in the brain found in the electrical brain activity. BCI researches are involved in the multidisciplinary field of study due to a need for not only knowledge of the electrical sensors, amplifiers or signal processing, but also brain anatomy and cognitive and sensory process in the brain as well.

Each of the BCI systems consists of the measuring instrument for measurement of the electrical brain activity (EEG amplifier), computer host for processing of the recorded signals and feature detection characteristic for specific BCI system. The electric brain activity measurement can be invasive (electrocorticography) with the electrodes placed directly on the surface of the brain, and non-invasive (electroencephalography) with the electrodes placed on top of the scalp. Despite better signal to noise ratio and better overall quality of the signal, invasive methods aren't suitable for the everyday use or researches. Signal processing and classification are directly depended on the task instructed to the subject to do. Examples can vary, from the simple ones (input commands for computer and video games, manipulations in the smart house, wheelchair control) to complex ones like robot or artificial prosthesis control. On Fig. 1 general scheme of the BCI system is shown.

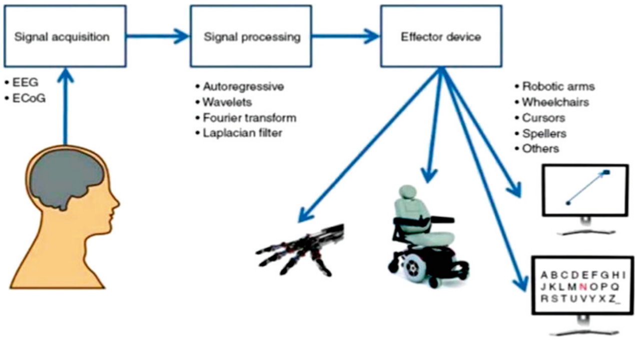

Fig 1. General scheme of brain-computer interface system (taken from [2] and modified)

BRAIN-COMPUTER INTERFACE BASED ON STEADY-STATE VISUAL EVOKED POTENTIALS

Steady-state visual evoked potentials

The steady-state visual evoked potentials (SSVEPs) belong to the visual evoked potentials group of brain activity. They are evoked as the brain reaction to current visual stimuli. Apart from the visual, there are auditory and somatosensory evoked potentials. SSVEPs occur with the flickering light stimulus. The amplitude is most expressed on the occipital brain region (visual cortex).

The characteristics of SSVEP are depended on the attributes of the stimuli (frequency and contrast). If the subject is presented with series of visual stimuli, which occur one after the other in uniform time intervals, the excited groups of the brain structures don't have time to return to the idle state. For stimuli, the black and white chessboard with alternating black and white fields is mostly used because of the strong contrast. As a result of such stimulus, high amplitude occurs in the frequency spectrum of the EEG signal from the occipital brain region, on the flickering frequency of stimuli. Scheme of BCI system with flickering chessboard as main stimuli is shown on Fig. 2.

CONTENTS

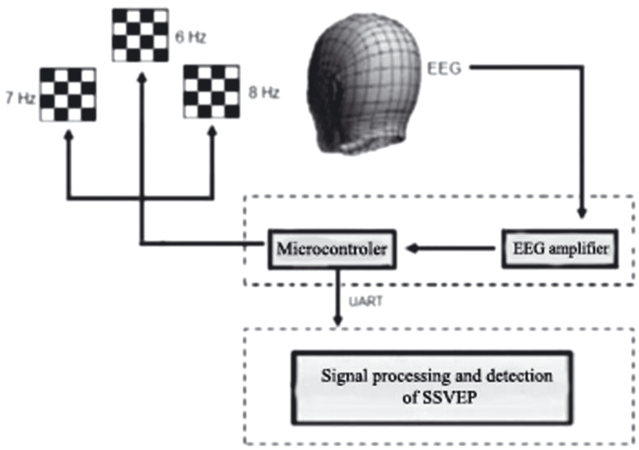

Fig 2. Scheme of BCI system with flickering chessboard

Detection and classification of eye gaze on chessboard

Brain-computer interface requires work in real time, so it is necessary to minimize the time of execution of the program code for feature extraction and classification of the eye gaze as much as possible. Given the short time of execution, Fourier transformation is selected as a method of analysis performed with Fast Fourier Transform (FFT) algorithm.

Before the Fourier transformation, over the previously filtered signal autocorrelation is carried out. The autocorrelation of the signal f (t) given by the formula:

$$R_{ff}(\tau) = \lim_{T\to\infty} \frac{1}{2T} \int_{-T}^{T} f(T) f(t-\tau)\, dt$$

Autocorrelation of the periodic signal is a periodic function of the same frequency as the signal, while autocorrelation of the aperiodic signal tends cancel out to zero for large movements [3]. Thereby, to decrease the influence of spontaneous brain activity in the EEG signal and to increase the influence of the periodic nature of the steady state evoked potential, autocorrelation is first used.

Classification of eye gaze on current chessboard can be performed by various methods such as machine learning and adaptive thresholding. In this case, a relatively rugged phenomenon is observed, so relative simple classification with thresholds at amplitudes of EEG spectrum at frequencies of chessboard oscillation and their harmonics is used.

Applications

Developed BCI can be applied in standard control and command applications, for example virtual keyboard. An interesting application is possible in smart homes, where such BCI, because of its robustness, can be used, for example in control of household lighting.

An important application of BCI system based on steady-state evoked potentials may be in video games for children with attention deficit disorder. Because of the need to subject to focus on stimulus, it is possible to design a game that would encourage concentration.

BRAIN-COMPUTER INTERFACE WITH ALPHA WAVE DETECTOR

Brain rhythms

Mental activities, emotional and psychological states, such as sleep, relaxation, solving of complex mathematical problems or discussions, are followed by different brain activity. Brain activity can be manifested in the form of brain rhythms (waves), called alpha (α), beta (β), delta (δ), theta (θ) and gamma (γ).

German neurologist Hans Berger first called perceived rhythmic EEG activity alpha waves. Alpha waves dominate in the occipital region of the brain and they appear in a state of relaxation. Their amplitude increases with eyes closed. The amplitude of alpha waves is not constant, but it changes in the shape of a spindle and then completely disappear and reappear after a few seconds. Alpha waves disappear during sleep and during enhanced cognitive activities (such as thinking, solving a problem). Alpha wave frequency range from 8 Hz to 12 Hz, while their amplitude is approximately equal to 50 μV.

Beta waves have lower amplitude than alpha waves and they occur mainly during increased brain activity (concentration, reflection, etc.). Also, they are dominant in patients experiencing anxiety. By opening the eyes alpha waves become blocked because the concentration of the patient increase and this causes the appearance of beta and disappearance of the alpha waves. Beta waves most commonly occur in the frontal and parietal region.

Theta waves and delta waves belong to the low frequency EEG spectra (<8 Hz) and have large amplitude relative to other waves. They occur in young children, or in a deep sleep in adults and may be an indication of abnormal brain disease.

Gamma waves are in the frequency range from 30 Hz to 100 Hz, and belong to the highest frequency range of the EEG waves. Until recently it was not seen as part of the EEG and they are only recently began to study more. Research shows that the brain enters the gamma state when high levels of processing information occurs.

In addition to the described dominant brain rhythms, mu rhythm has been recognised, also known as the Roland rhythm. It is located in the frequency and amplitude range of alpha rhythm, but topology and physiological character is different from the alpha. Mu rhythm is associated with imagining movement and motor movements. It is used for research of motor and sensory functions of the body, as well as in the rehabilitation of epileptic seizures.

The scientific community agrees that the alpha waves are an important source of knowledge and information on the functioning of the human brain and are often an inspiration to numerous studies of human behaviour, learning and concentration. Alpha waves get extra attention with the advent of biofeedback theory, which claims that it is possible to, at least partially, control the bodily processes that are normally controlled by the autonomic nervous system. Research of the alpha rhythm in conjunction with the biofeedback method presently shows interesting results in the treatment of depression, and phobias. In recent years, the alpha waves are increasingly associated with meditative states, while at the same time the positive correlation between high levels of alpha waves and creativity, better memory and faster problem solving is highlighted. Therefore, scientists are trying to find a method that would allow the conscious control of alpha waves [4].

Wavelet transform detection of alpha waves

The recorded EEG signal is first filtered with 4th order bandpass Butterworth filter with the limits f_1=3.5 Hz and f_2=40 Hz in order to avoid interference with the city power network noise. After pre-processing, signal feature extraction and detection of alpha rhythm by applying wavelet transformation is implemented. Wavelet mother function is the most important parameter in the analysis of the EEG signal because feature extraction signal depends on the correlation of the analysed signal and wavelet function. A group of orthogonal wavelet functions is chosen as one of the groups whose prototypes give the best results in the detection of alpha rhythm of the EEG signal. From the group of orthogonal functions wavelets Daubechies, Symlets and Coiflets are chosen and tested with Daubechies function of order 4 [5], Symlets of order 9 [6] and Coiflets the order of 5 [7].

By applying the discrete wavelet transform (DWT) details of eight levels are extracted. With sampling rate of 200 Hz, details of the fourth level (D4) includes the frequency band from 6.25 to 12.5 Hz. This frequency bands corresponds to that of alpha waves and the coefficients of these details are taken for further processing. On detail coefficient two methods of decision-making are applied to decide if the alpha waves are present. Both methods are based on the maximum absolute value of the wavelet transformation coefficients $M_j(T)$. Formulas for calculation of thresholds are given as:

$$Prag_1 = mean(M_j) + 2 \cdot std(M_j)$$

$$Prag_2 = 1.5 \cdot std(M_j)$$

where *mean*() i *std*()are functions of arithmetic mean and standard deviation, and M_j is defined as:

$$M_j(T) = \max\left|C_T(j)\right|$$

where C_T (*j*) is coefficient of level *j* given with wavelet transformations of EEG signal segment in given time T.

To test the method, the sections of 200 samples (1 second) of the signal are used. Slices were taken every 100 samples (half a second). If the 25% coefficient of wavelet transformation are larger than the set threshold, the presence of alpha waves is defined as positive. Otherwise, the presence is defined negative.

Based on the literature [8], we analysed the method of applying the Fourier transform to the previously calculated coefficients of wavelet transformation D4. The exact boundaries of the frequency band covered in detail depend on the prototype used wavelet functions, as well as the number of levels of decomposition. Therefore, the Fourier analysis can analyse in detail the content of component D4 and examine whether it contains, in addition to the alpha rhythm, any signals of other frequencies. With simple algorithm, only the value of the spectrum belonging frequencies 8-13 Hz are extracted and the power spectrum for an isolated area is calculated:

$$P(T) = \sum_{f=8}^{13} \left|X_T(f)\right|^2$$

The resulting power spectrum is normalized to the values between [0.1] in order to facilitate a decision on the threshold value. Threshold is set to be 0.25. If the total power of calculated standardized spectrum of segment is greater than 0.25 presence of alpha rhythm is defined positively, otherwise or negatively.

Applications

Biofeedback is a technique of treatment with which the patient learns to control the internal bodily processes which are normally automatically controlled by the autonomous nervous system (e.g. heart rate, blood pressure, muscle tension, body temperature, and EEG activity). By using EEG recording is possible to get feedback in real time on the concentration of alpha waves in the overall brain activity, which is an indication of the current calmness and relaxation. Currently the most popular application of biofeedback techniques if for meditation, because it has been observed a significant increase in the concentration of alpha waves during deep meditative state. Biofeedback techniques has found its application in the treatment of phobias, depression, and calming hyperactive children and in practice with children with speech difficulties. Psychologists also found the application of alpha waves in the training of soldiers, to train their ability to increase the concentration of alpha waves successfully if they undergo lie detector. Probably the most interesting application of biofeedback techniques today is in business environment of high risk. In fact, studies have shown that the concentration of alpha waves increases by as much as 25% before the respondent makes a mistake, then again observed a significant decrease in their concentration when the subject becomes aware of such errors. This correlation is important in high-risk occupations (e.g., air traffic controllers). By using biofeedback methods, we can alert in time when their concentration falls or when they start automated and unknowingly perform a task [9]. In addition to these, biofeedback application will find benefit in many other aspects of life and business, especially when it comes to still unexplored characteristics and effects of alpha waves. Therefore, reliable and fast extraction of alpha rhythm of the entire EEG signal is of great importance.

BRAIN-COMPUTER INTERFACE BASED ON MOTOR IMAGERY

Brain activity during motor imagery

Two types of brain activity occur during the execution of movement (a similar activity occurs during the motor imagery [10]): movement related cortical potentials (MRCPs) and changes in the amplitude of sensorimotor rhythms (SMRs).

The primary somatosensory cortex is in the anterior part of the parietal lobe, while the primary motor cortex is located at the posterior part of the frontal lobe, separated by large fissure called central sulcus. Fig. 3 shows the division of the brain into the lobes and parts responsible

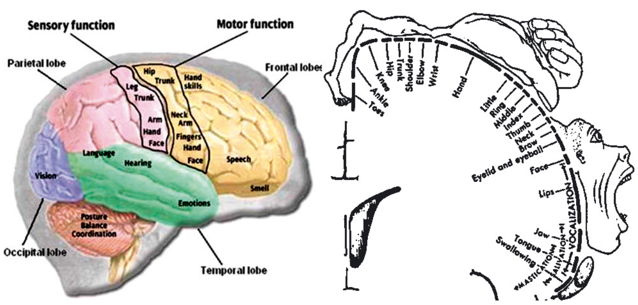

Fig 3. Functionality of different parts of the brain (left) and homunculus of motor (right) (taken [11])

for sensory and motor functions.

A more detailed breakdown of motor cortex is shown on the left side of Fig. 3, and it is called the homunculus (Latin for "little man"). Fig. 3 shows that some part of the body has a different surface area of regions responsible for its control. Both feet have relatively small representation in the primary motor cortex, while the hands have relatively large. The reason for this lies in the complexity of the movement that we can perform with your fingers, unlike those with those. The importance of this in the context of the brain-computer interface is in choosing the parts of the body with which we control the BCI. Only the part of the body with enough large representation on the motor cortex provide useful control signals. In addition, the activity of the hand is

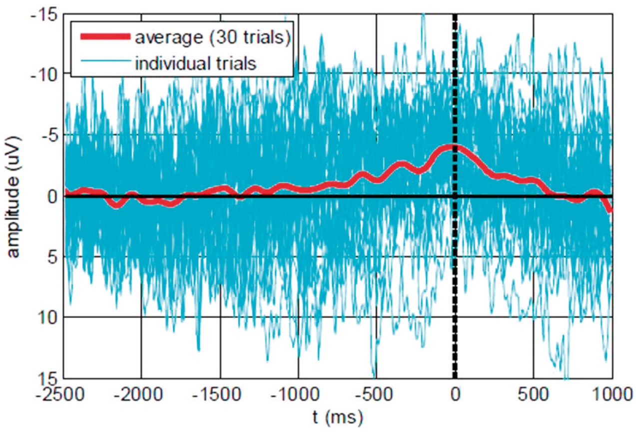

Fig 4. Averaged MRCP (red) i individual trials of EEG signal (blue) (taken from [11])

read on the contralateral hemisphere of the brain (left arm activity occurs in the right hemisphere, and vice versa). That way it is easily to distinguish which participates in the control, while the differentiation of the activity of the left and right foot is a difficult task.

In these regions, MRCP emerge during the planning, preparation and execution of movement. For causing visible activity of MRCP recorded with EEG, it is necessary to repeat the same movement several times after which the recorded brain activity is averaged (Fig 4.). Small amplitudes (a few microvolts) in relation to the spontaneous brain activity, together with a large variability in time relative to the movement, makes MRCP unsuitable for use as control signals in the BCI systems since it takes time for extraction of recognisable waveform.

Somatosensory rhythms show two types of amplitude modulation when performing movements: evoked desynchronization (ERD) and evoked synchronization (ERS). Within the frequency band of a mu rhythm, evoked desynchronization occurs as amplitude attenuation during the preparation and execution of movement, while evoked synchronization occurs in the beta frequency band as an amplitude gain, after the movement. Unlike traditional evoked potentials (obtained by averaging), which can be observed as the major series of postsynaptic responses of pyramidal neurons activated to some stimuli, ERD / ERS can be observed as a change in one or more parameters which control the oscillations of the neural structures. These changes are not phase related to the event, so time-frequency analysis is needed.

Time-frequency analysis of evoked desynchronisation and synchronisation

To extract features characteristic for the evoked synchronisation or desynchronisation, it is necessary to carry out time-frequency (TF) analysis. Often the simple bandpass filtering of bandwidth of interest is used. By comparing the power spectrum with baseline levels averaged prior to the execution of movement it is possible to extra-

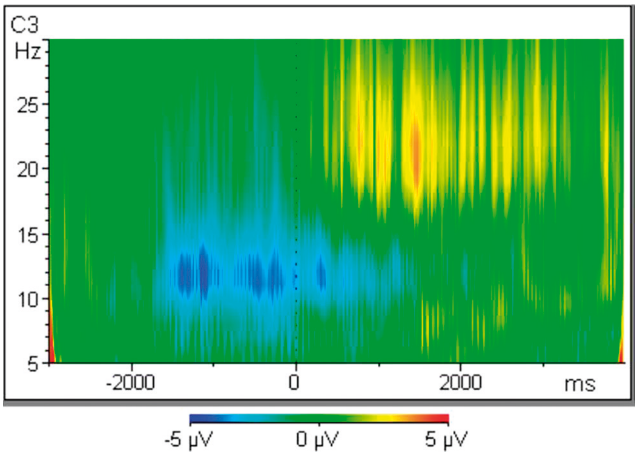

Fig 5: Evoked desynchronisation and synchronisation during right hand movement (recorded on C3 electrode)

ct the appearance of desynchronisation or synchronisation (Fig. 5).

It is shown that by using more complex mathematical methods, such as Hilbert-Huang transformation, can improve the quality of classification. Hilbert-Huang transformation for real signals is given by:

$$h_H(t) = H\left[x(t)\right] = \frac{1}{\pi} PV \int_{-\infty}^{\infty} \frac{x(\tau)}{t-\tau} d\tau$$

Because of the large signal individuality of each subject, greater accuracy is achieved by selecting individual time and frequency window in relation to the moment of the beginning of movement imaging. In Fig. 6, the different classification accuracy for different time windows and frequency bands is shown.

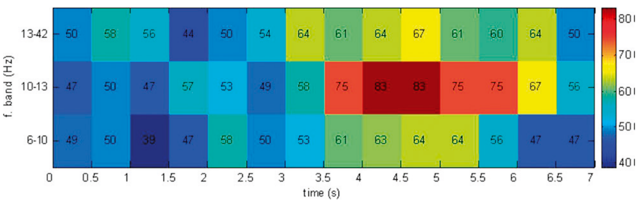

Fig 6: Classification accuracy for different time-frequency bins(taken from [11])

Applications

The use of this BCI system feels the most natural in the control applications, where imagining particular movement commands (e.g., imagining the movement of left hand moves a wheelchair to the left). An interesting application of movement imagery is in the rehabilitation of patients of a stroke. Imagining movement provides one mode to rehabilitation during training movement [12]. By applying the BCI system it is possible to give feedback to the patient in rehab, which would speed up his recovery.

Literature

[1] Sanei S.,Chambers J.A. „EEG Signal Processing, John Wiley & Sons Ltd., University Cardiff, 2007.

[2] https://www.slideshare.net/asertseminar/bci-32898921, March,1,2017.

[3] Lončarić, S., Random Processes in Systems – lectures, University of Zagreb Faculty of Electrical Engineering and Computing, Zagreb, 2008.

[4] Zavacki T., Extraction of alpha rhythm from EEG signal, Master Thesis, University of Zagreb Faculty of Electrical Engineering and Computing, Zagreb, 2016.

[5] Prachi Parikh i Evangelia Micheli-Tzanakou. Detecting drowsiness while driving using wavelet transform. Bioengineering Conference, 2004. Proceedings of the IEEE 30th Annual Northeast, ppe 79–80. IEEE, 2004.

[6] Noor Kamal Al-Qazzaz, Sawal Hamid Bin Mohd Ali, Siti Anom Ahmad, Mohd Shabiul Islam, i Javier Escudero. Selection of mother wavelet functions for multichannel EEG signal analysis during a working memory task. Sensors, 15(11):29015–29035, 2015.

[7] Ahmad Taher Azar, Valentina E Balas, i Teodora Olariu. Classification of EEG-based brain–computer interfaces. U Advanced Intelligent Computational Technologies and Decision Support Systems, ppe 97–106. Springer, 2014.

[8] Maan M. Shaker. EEG waves classifier using wavelet transform and Fourier transform. International Journal of Medical, Health, Biomedical, Bioengineering and Pharmaceutical Engineering, 1(3), 2007.

[9] Michael Hardy, Hgamboa, i et. al. Alpha wave. https://en.wikipedia.org/wiki/Alpha_wave?oldid=687824617, 2015.

[10] R. Beisteiner, P. Höllinger, G. Lindinger, W. Lang, and A. Berthoz, "Mental representations of movements. Brain potentials associated with imagination of hand movements," Electroencephalogr. Clin. Neurophysiol., vol. 96, no. 2, pp. 183–93, 1995.

[11] Jerbić, A.B., Extraction of movement related oscillatory changes from electroencephalogram with application to brain-computer interface, doctoral thesis, University of Zagreb Faculty of Electrical Engineering and Computing, Zagreb, 2015.

[12] McEwen, Huijbregts, Ryan, Polatajko. Cognitive strategy use to enhance motor skill acquisition post-stroke: a critical review. Brain Inj, 23 (263-277), 2009.

Magdalena Krbot Skorić

INVASIVE EEG MONITORING AND ITS APPLICATION IN THE SURGICAL TREATMENT OF PATIENTS WITH PHARMACORESISTANT EPILEPSY

Laboratory for Cognitive and Experimental Neurophysiology, Department of Neurology, University Hospital Center Zagreb

Epilepsy is one of the most common neurological diseases. It manifests itself as a disorder of the central nervous system that is caused by repetition of abnormal, excessive and synchronous neural discharge [1]. Such neural discharges are clinically manifested with epileptic seizures, and a diagnosis of epilepsy is made if seizures are repeated two or more times. Possible causes of epilepsy are various: genetic disorders, birth trauma, anoxia, infection, traumatic head injury, stroke, and many others, but in approximately one third of patients the cause of epilepsy is unknown. Seizures have a major impact on the health of patients - each new seizure could cause micro damage to the brain and the patients could possibly be hurt during the attack. Also, seizures affect the quality of life of patients - often people suffering from epilepsy have problems with employment and promotion opportunities. For many of them a driver's license could be denied, and also there is significant effect on the social life because of the frequent isolation from friends and constant uncertainty whether the seizure will happen.

Consequently, the main goal of treatment in patients with epilepsy is partial or complete reduction of seizures. The treatment is usually pharmacological (anti-epileptic drugs – AED), with one, two or more AEDs. However, there are great difficulties with the pharmacoresistant form of epilepsy, in which seizures continue after two years of treatment and / or after unsuccessful treatment with a combination of two to three antiepileptic drugs [2]. According to available literature, in about 50% of people with epilepsy only one AED is sufficient for complete seizure reduction, but the problem is that about 36% of patients have pharmacoresistant form of epilepsy [3].

Patients with pharmacoresistant epilepsy are treated with invasive methods, such as vagus nerve stimulation or one of neurosurgical procedures. The vagus nerve stimulation in combination with drug therapy can be very beneficial. For the purpose of stimulation, the vagus nerve stimulator is implanted in the left chest and the wire electrode is wrapped around the left vagus nerve [1]. The vagus nerve stimulator works on the assumption that stimulation of the nerve vagus sensory fibres can desynchronize cortical activity and reduce the incidence and severity of the epileptic seizures [1]. Another possibility for the treatment of pharmacoresistant epilepsy is surgical resection of epileptic regions of the brain. It is recommended to perform surgical resection as soon as it is determined that it is the only possible treatment , because the long term, frequent and severe attacks can lead to serious damage of the brain tissue and significantly affect cognitive and motor abilities of patients with epilepsy.

The result of the surgical resection is removing one part of the brain, and is of great importance that before the resection areas responsible for the generation of epileptic seizures are localized with great precision, but it is of equal importance to determine whether these areas can be removed without fatal consequences to neurological and cognitive function. For this purpose, detailed preoperative assessment designed to accurately predict the outcome of the surgery and to preserve the quality of life of patients is performed.

The preoperative assessment and invasive monitoring is being performed since 2010 at the Department of Neurology, University Hospital Center Zagreb, as part of the Referral Centre for Epilepsy of the Ministry of Health of the Republic of Croatia, led by Prof. Sanja Hajnšek. A multidisciplinary team consisting of neurologists, neurosurgeons, neuroradiologists and medical engineers participates in this extremely demanding procedure. The procedure is highly personalized. It requires a high degree of expertise and knowledge, and careful selection of patients based on a detailed preoperative evaluation (determination of the semiology of the seizures, epileptogenic lesion detection, and detection of the epileptogenic zone [4]). After the selection of patients, the preoperative evaluation is performed, which precedes the neurosurgical procedure of removing epileptic tissue.

Preoperative evaluation can be divided into two phases: Phase I - non-invasive procedures and Phase II - invasive procedures. Phase I includes: preoperative neuropsychological and neurocognitive testing, cognitive evoked potentials, EEG polygraph video recording, magnetic resonance (MR - 3T), MR volumetric analysis (particularly hippocampal sclerosis), functional MR recording with MR tractography, MR spectroscopy, and 'postprocessing' MR methods. Examples of the results of the MRI are shown in Figure 1.

Also, the functional imaging methods are performed, such as PET (positron emission tomography), SPECT (single-photon emission computed tomography) and SISCOM (Subtraction ictal SPECT co-registered to the MR) which presents comparison of ictal and interictal SPECT co-registered to MR (Figure 2).

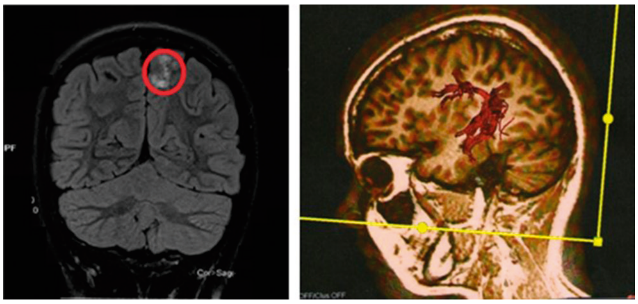

Fig. 1: a) MR-3T with marked area of the lesion and b) functional MRI with a location of *Fasciculus arcuatus*

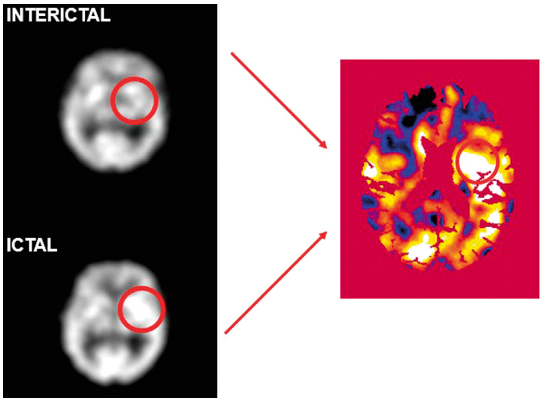

Fig. 2: SISCOM – subtraction of ictal from interictal SPECT and correlation with MRI; the connection between functional and morphological information, the area of the epileptogenic activity is marked

Based on the results obtained in the Phase I of the preoperative evaluation, the more detailed location of the area of interest is known, which is necessary for the Phase II. The Phase II consists of invasive procedures that will provide detailed information about the exact location of the epileptogenic tissue that has to be removed. Also, the Phase II emphasizes the value of the invasive monitoring, because it shows what would happen if the epileptic tissue is removed and what impact it will have on the patient's quality of life.

Invasive stage of the preoperative evaluation consists of the Wada test and invasive EEG monitoring. In the Wada test one hemisphere of the brain is temporarily anesthetized with certain amount of anaesthetic in order to see what impact the absence of one hemisphere would have on motor and cognitive functions of patients [5]. Although the Wada test is the golden rule of lateralisation of speech function, it is important to assess for each patient the ratio between risks and complications related to this method and the postoperative benefit.

Invasive EEG monitoring is a procedure that determines the exact location of the epileptic zone for the neurosurgical resection, but also at the same time maps areas of the cortex responsible for speech, cognitive, motor and sensory functions. Special electrodes for invasive monitoring are implanted into the patient, and EEG activity is monitored over several days (24 hour a day) with a 128-channel EEG amplifier. Based on the data obtained from methods in Phase I, for each patient it is determined which electrodes are required for invasive monitoring and precise location where electrodes should be implanted. There are several types of electrodes, they can vary in their form and way of implantation (surface electrodes or deep electrodes). Figure 3 shows a schematic view of the location of the electrodes (a) and a realistic view of the location (b). From the data obtained from invasive monitoring about the location of the epileptogenic zone, neurosurgeons determine the trajectory of the neurosurgical resection.

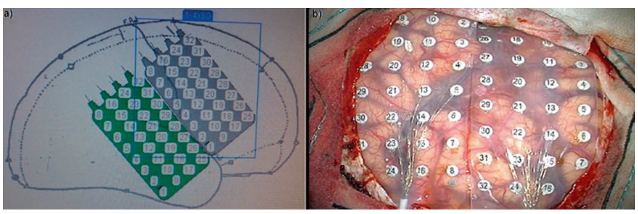

Fig. 3: Electrode scheme (a) and realistic representation (b)

Anatomy of the brain (gyrus and sulci) and the organization of brain functions are specific for each person. Therefore it is necessary to determine whether the area of the epileptogenic zone, which is planned for neurosurgical resection, also contains areas of the brain associated with motor control, sensors, and cognitive functions or speech. The "brain mapping", whose main role is to preserve the quality of life of the patient after surgery, should be performed for every patient. "Brain mapping" is performed with the cortical stimulator and a battery of tests, where electrical stimulation of individual electrodes simulates the disabling brain tissue beneath these electrodes to determine what would happen if that piece of brain tissue is removed. The battery of tests is very carefully selected with the purpose to examine cognitive, motor and sensory functions. During the procedure, the stimulation is performed with two by two electrodes and the intensity of the stimulation is gradually increased. During the test, it is important to record all the changes that the patient feels regarding the motor, sensory, and cognitive functions and speech.

Based on the results of the testing, for each patient the functional brain map is defined (shown in Figure 4). The functional brain map is very important for the planning of the neurosurgical resection because it provides insight into which motor, sensory or cognitive functions are related to the area of the epileptogenic zone, and which part of the brain tissue could be removed without adverse consequences for the patient.

Based on the information obtained from the invasive monitoring, the neurosurgical removal of epileptic tissue is performed.

The success of the procedure is evaluated according to the quality of life of the patient after the surgery, measured with a degree of the reduction of epileptic seizures while preserving all motor, sensory and cognitive functions.

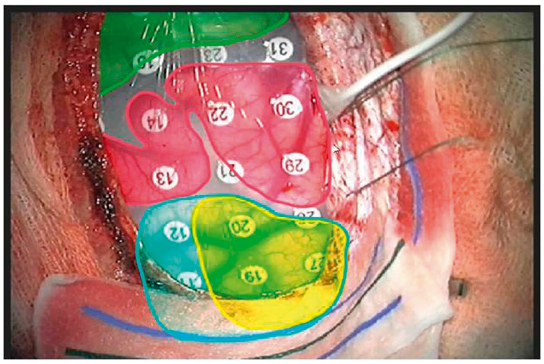

Fig. 4: The functional brain map: individual presentation of sensory and motor areas related to the epileptogenic zone; red line – primary sensor area, green line – primary motor area, yellow line – area of lesion, blue line – epileptogenic area

UNIVERSITY HOSPITAL CENTER ZAGREB

Department of Neurology

Prof. Sanja Hajnšek, MD, PhD
Prof. Zdravka Poljaković, MD, PhD
Prof. Željka Petelin Gadže, MD, PhD
Prim. Sibila Nanković, MD
Vlatko Šulentić, MD, MSc
Magdalena Krbot Skorić, PhD, Dipl Eng
Andreja Bujan Kovač, MD
Ivana Čajić, MD

Department of Neurosurgery

Assist. Prof. Goran Mrak, MD, PhD
Andrej Desnica, MD, PhD

Department of Radiology

Prof. Marko Radoš, MD, PhD
Assist. Prof. Milan Radoš, MD, PhD
Goran Pavliša, MD, PhD
David Ozretić, MD, PhD

References:

[1] Vesna Brinar i sur., Neurologija za medicinare. Zagreb, HR: Medicinska naklada, 2009

[2] G. Gelziniene, M. Endziniene, N. Vaiciene, M. R. Magistris, M. Seeck, "Presurgical evaluation of epilepsy patients", Medicina (Kaunas), vol. 44, pp. 585-592, 2008

[3] P. Kwan, M.J. Brodie, "Early identification of refractory epilepsy", N Engl J Med., 342(5), pp. 314-19, 2000

[4] H.O. Luders, J. Jr. Engel, C. Munari, "General principles", in: J. Jr. Engel, Ed. Surgical treatment of the epilepsies, 2nd ed. Raven Press: New York, pp. 137-53, 1993

[5] B. Abou-Khalil, "An update on determination of language dominance in screening for epilepsy surgery: the Wada test and newer noninvasive alternatives", Epilepsia, vol. 48(3, pp. 442-455), 2007

Luka Crnošija[1], Magdalena Krbot Skorić[2], Tereza Gabelić[2], Mario Habek[1,2]

THE ROLE OF EVOKED POTENTIALS IN MULTIPLE SCLEROSIS

[1] University of Zagreb, School of Medicine
[2] University Hospital Centre Zagreb, Department of Neurology

INTRODUCTION

Multiple sclerosis (MS) is chronic inflammatory demyelinating disease of the central nervous system (CNS), and the leading cause of disability in young adults. Considering that inflammation can affect any part of the CNS, this disease can present itself with myriad of symptoms, thus it is sometimes called "the disease with thousand faces". Symptoms that patients develop are caused by inflammation leading to demyelination (i.e. the disruption of the myelin sheath) which results in slowing of impulse conduction through neuronal pathways, and functional deficits in systems innervated by demyelinated nerve fibres (e.g. locomotor and sensory system). For example, one of the more important and frequently affected functions, particularly in patients with longer disease duration, is walking. According to North American Research Committee on Multiple Sclerosis registry 45% of MS patients aged between 18-64 years use some form of mobility devices (1). Moreover, MS is the leading cause of wheelchair use in this age group (2). It is only recently that a wider range of drugs for treating MS became available, and they can be divided in two groups, i.e. the first and second line. The second line of treatment includes more efficient drugs, but with more severe possible side-effects. This line of treatment is used in patients with more aggressive disease course or in patients who were unresponsive to the first line treatment.

Considering this wider range of therapies available today, one of the challenges is to estimate which therapy is the best choice for specific patient taking into account his or her current health state and factors which may indicate future course of disease in this patient. In addition to neurological examination, brain and cervical spinal cord magnetic resonance imaging (MRI) is typically used in order to gain insight into patients' current state and disease activity. Studies have shown that demyelinating lesions detected with the MRI in some parts of the CNS, such as the brainstem, carry higher risk for worse disease course (3-5). On the other hand, it is also known that MRI findings do not always correlate with clinical finding, meaning that patient may have some symptoms, but no corresponding lesions are evident on MRI. The latter is referred to as the clinico-radiological paradox (6), which is particularly emphasized in the brainstem region (7). Thus there is a need for additional methods and tools for assessing different neurological system, and evoked potentials are one of these methods.

EVOKED POTENTIALS

Evoked potentials (EP) are a group of different slightly different diagnostic procedures, but all share the same principle; the response of specific neural pathway to appropriate stimulation is recorded and analysed. Using this principle, numerous neural pathways and systems can be inspected, for example somatosensory system (somatosensory evoked potentials – SSEP), vestibular (vestibular evoked myogenic potentials – VEMP), visual (visual evoked potentials – VEP), auditory (brainstem auditory evoked potentials – BAEP), and motor system. For instance, one of the most commonly used types of stimuli is the electric impulse. The electric impulse is sensed by sensory nerve fibres which then emit the information from the place of stimulation (e.g. ankle) to cerebral sensory cortex. The sensory information is transduced as a transient "travelling" change of the electric potential on the membrane of nerve cells, and these changes in the electric potential (so called evoked potentials) can be recorded via electrodes placed along the examined neural pathway. Several parameters of the recorded response are analysed (i.e. the amplitude, latency and morphology of the response) and compared to the referent values of healthy population. The name of the recorded response (the so called "wave") usually contains information on the polarity of electric potential change (i.e. positive (P) or negative (N)), and the approximate time (measured in milliseconds) needed for the evoked potential to travel the distance from the site of stimulation to the measuring electrode in healthy population. For example, P100 wave describes positive change of the electric potential measured at 100 ms after the stimulation.

THE ROLE OF EVOKED POTENTIALS IN MULTIPLE SCLEROSIS

The role of EPs in the assessment of MS patients changed over time, and with the emergence of new technologies, especially the magnetic resonance imaging (MRI), EPs were unjustifiably considered less useful. In recent years EPs are becoming increasingly important in MS diagnostics, which is clearly reflected in the fact that visual evoked potentials became enlisted in the new criteria for diagnosing MS (8). In contrast to imaging methods, such as the MRI, EPs can give us insight in the actual function of the specific neural pathway. Since demyelinating inflammation of the central nervous system is the hallmark of MS, typical finding on EPs in MS are prolonged latencies of responses. Other common findings are decreased amplitudes or even absence of response depending on the degree of damage of myelin sheaths or neurons themselves.

VISUAL EVOKED POTENTIALS (VEP)

Considering that the first manifestation of MS in about 20% of patients is the inflammation of the optic nerve (i.e. optic neuritis – ON), VEPs are one of the most commonly used methods among Eps (9). Typical finding on VEP in the acute phase of ON are prolonged latencies (Figure 1) and reduced amplitudes of the responses. Although the amplitudes of VEP responses return to normal some time after the ON, the latency of the response usually remains prolonged. The sensitivity for identifying a patient who experienced ON some time in the past is 77-100% (10, 11). It is for this reason that VEPs can be used for estimating whether the patient fulfils one of the criteria for diagnosing MS, i.e. the dissemination in time.

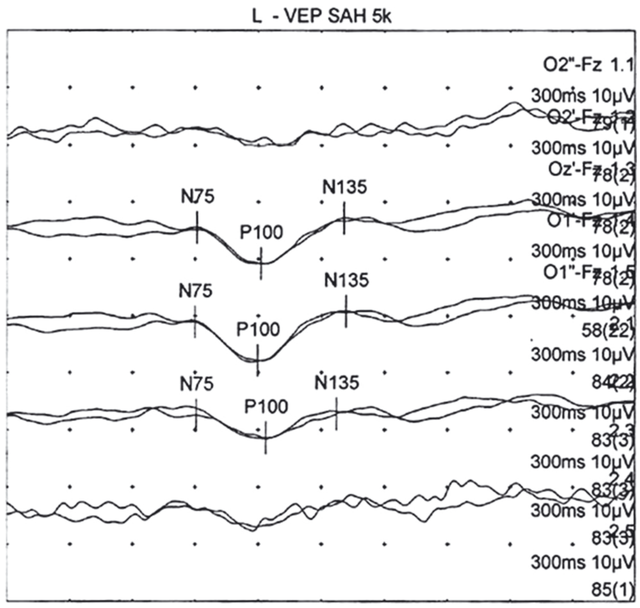

Fig. 1: An example of prolonged latency of visual evoked potential response. P100 wave was recorded more than 120 ms after the stimulation.

SMATOSENSORY EVOKED POTENTIALS (SSEP)

SSEPs of upper and lower extremities can give us insight in the function of somatosensory pathway in dorsal columns of the spinal cord and thalamo-cortical sensory system in the brain. The value of evoked potentials as a method lies primarily in their ability to detect subclinical damage of the nervous system, and SSEPs of lower extremities (Figure 2) are considered to be one of the most valuable methods among Eps (12). Studies have shown that SSEPs of lower extremities can detect the damage of spinal cord somatosensory system in as much as 80% of MS patients without corresponding clinical symptoms (13).

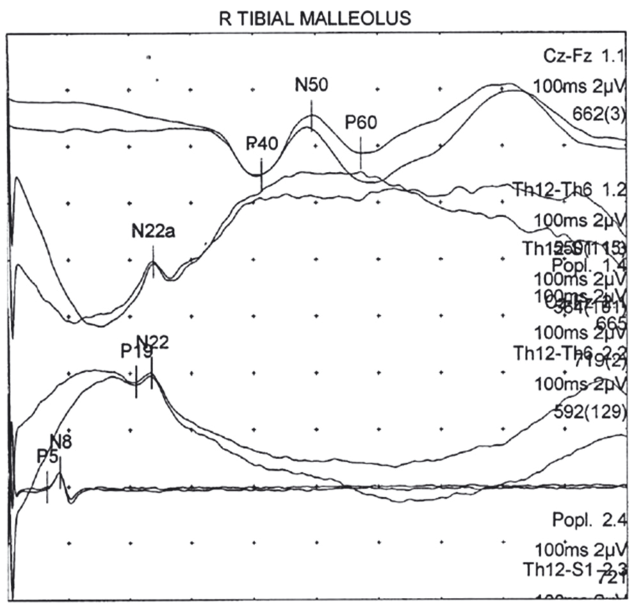

Fig. 2: An example of normal response recorded during SSEP of lower extremities. In this diagnostic procedure tibial nerve is stimulated via electric impulse at the level of ankle, and the responses are recorded at several spinal cord levels, as well as over sensory cortex of the brain.

BRAINSTEM EVOKED POTENTIALS

Brainstem auditory evoked potentials (BAEP) and vestibular evoked myogenic potentials (VEMP) evaluate the function of auditory and vestibular system (i.e. system responsible for sense of balance) at the level of the brainstem. While BAEP is one of the least sensitive methods among EPs (14), VEMP has been shown to be superior compared to BAEP, as well as compared to neurological exam and brain MRI (15). SSEP of the trigeminal nerve has also proven to be valuable in detecting lesions of upper portion of the brainstem (i.e. the mesencephalon) in MS patients (16).

THE EVOKED POTENTIAL SCORE

Considering that by using different EP methods various parts of the nervous system can be evaluated, an idea to create an indicator of the global state of function of MS patients' nervous system was born. By marking every VEP and BAEP response, and motor and SSEP responses of upper and lower extremities according to hypothetical degree of damage, and summing-up all of the result, Leocani et al. developed the so-called evoked potential score (EP score). In this model normal responses were marked as 0, prolonged latencies as 1, abnormal morphologies of waves was marked as 2, and an absence of response was marked as 3 (17). In this longitudinal study patients were followed-up for about three years, and EP score correlated well with neurologist's clinical findings, but it also showed predictive value. Subjects who had EP score higher than the median of this sample had 72.5% higher risk for clinical worsening in the control period. Also, another retrospective study with longer follow-up period confirmed the predictive value of EP score (18).

One of the shortfalls of both studies is that only BAEP was used to evaluate the function of the brainstem. This is especially important considering the before-mentioned correlation between brainstem lesions and higher risk for worse course of the disease. It is for that reason that the VEMP score was developed. VEMP score correlated well with both clinical and MRI findings of brainstem integrity, and it also had independent predictive value of clinical state of MS patients (19, 20). The value of VEMP score as a predictor of disease course is still a matter of study.

CONCLUSION

Evoked potentials are very valuable neurophysiological method in diagnostics and follow-up of MS patients. The biggest advantage of EPs is the ability to detect subclinical damage of the nervous system. Also, considering that this method gives us information about the functional state of the inspected neural pathway, it is complementary to MRI when evaluating MS patients. Some studies have shown that by using a battery of EPs can be used to gain better understanding of the current state of individual MS patient, and can even be used to identify patients at higher risk of disease progression. This predictive value is especially important when deciding which therapy is the most suitable one for specific MS patient.

References

[1] Kister I, Chamot E, Salter AR, Cutter GR, Bacon TE, Herbert J. Disability in multiple sclerosis: a reference for patients and clinicians. Neurology. 2013; 80:1018-24.

[2] Kaye, HS, Kang T, LaPlante MP. Mobility Device Use in the United States. National Institute on Disability and Rehabilitation Research, US Department of Education, 2000. (http://www.disabled-world.com/pdf/mobility-report.pdf) (accessed 8.01.2017.)

[3] Filippi M, Horsfield MA, Morrissey SP *et al.* Quantitative brain MRI lesion load predicts the course of clinically isolated syndromes suggestive of multiple sclerosis. *Neurology* 1994;44:635-641.

[4] Sailer M, O'riordan JI, Thompson AJ *et al.* Quantitative MRI in patients with clinically isolated syndromes suggestive of demyelination. *Neurology* 1999;52:599-606.

[5] Minneboo A, Barkhof F, Polman CH, Uitdehaag BM, Knol DL, Castelijns JA. Infratentorial lesions predict long-term disability in patients with initial findings suggestive of multiple sclerosis. *Arch neurol 2004;*61;217-221.

[6] Barkhof F. The clinico-radiological paradox in multiple sclerosis revisited. *Curr opin neurol* 2002;15:239-245.

[7] Zadro I, Barun B, Habek M, Brinar VV. Isolated cranial nerve palsies in multiple sclerosis. *Clin Neurol Neurosurg* 2008;110:886-888.

[8] MAGNIMS Study Group. MRI criteria for the diagnosis of multiple sclerosis: MAGNIMS consensus guidelines. Lancet Neurol. 2016; 15:292-303.

[9] Brownlee WJ, Miller DH. Clinically isolated syndromes and the relationship to multiple sclerosis. J Clin Neurosci. 2014; 21:2065-71.

[10] Movassat M, Piri N, AhmadAbadi MN. Visual Evoked Potential Study in Multiple Sclerosis Disease. Iran J Ophthalmol 2009;21:37-44.

[11] J Palace. Making the diagnosis of multiple sclerosis. J Neurol Neurosurg Psychiatry 2001;71:ii3-ii8.

[12] Djuric S, Djuric V, Zivkovic M, Milosevic V, Jolic M, Stamenovic J, Djordjevic G, Calixto M. Are somatosensory evoked potentials of the tibial nerve the most sensitive test in diagnosing multiple sclerosis? Neurol India 2010;58:537-41.

[13] Kraft GH, Aminoff MJ, Baran EM, Litchy WJ, Stolov WC. Somatosensory evoked potentials: clinical uses. AAEM Somatosensory Evoked Potentials Subcommittee. American Association of Electrodiagnostic Medicine. Muscle Nerve 1998;21:252-8.

[14] Comi G, Leocani L, Medaglini S, Locatelli T, Martinelli V, Santuccio G, Rossi P.Measuring evoked responses in multiple sclerosis. Mult Scler. 1999; 5:263-7.

[15] Skorić MK, Adamec I, Mađarić VN, Habek M. Evaluation of brainstem involvement in multiple sclerosis. Can J Neurol Sci 2014;41:346-9.

[16] Krbot Skorić M, Adamec I, Crnošija L, Gabelić T, Barun B, Zadro I, Butković Soldo S, Habek M. Tongue somatosensory evoked potentials reflect midbrain involvement in patients with clinically isolated syndrome. Croat Med J 2016; 57:558-565.

[17] Leocani L, Rovaris M, Boneschi FM, Medaglini S, Rossi P, Martinelli V, Amadio S, Comi G. Multimodal evoked potentials to assess the evolution of multiple sclerosis: a longitudinal study J Neurol Neurosurg Psychiatry 2006;77:1030-1035.

[18] Invernizzi P, Bertolasi L, Bianchi MR, Turatti M, Gajofatto A, Benedetti MD. Prognostic value of multimodal evoked potentials in multiple sclerosis: the EP score. J Neurol 2011;258:1933-9.

[19] Gabelić T, Krbot Skorić M, Adamec I, Barun B, Zadro I, Habek M. The vestibular evoked myogenic potentials (VEMP) score: a promising tool for evaluation of brainstem involvement in multiple sclerosis. Eur J Neurol 2015;22:261-9, e21.

[20] Crnošija L, Krbot Skorić M, Gabelić T, Adamec I, Habek M. Vestibular evoked myogenic potentials and MRI in early multiple sclerosis: Validation of the VEMP score. J Neurol Sci. 2017; 372:28-32.

Magdalena Krbot Skorić[1], Mario Cifrek[2], Igor Krois[2], Ana Branka Jerbić[3], Velimir Išgum[3]

VIBRATORY EVOKED POTENTIALS

[1] Department of Neurology, University Hospital Centre Zagreb, Zagreb, Croatia
[2] Faculty of Electrical Engineering and Computing, University of Zagreb, Zagreb, Croatia
[3] University of Zagreb, Zagreb, Croatia

The sense of vibration forms a part of proprioceptive sense and difficulties related to the sense of vibration are frequent indicators of neurological disorders. In classical clinical practice the sense of vibration is typically examined using a vibratory fork. The vibratory fork does not provide quantitative information about the sense of vibration, obtained information is subjective and the method is not applicable to people suffering from disorders of consciousness and little children [1]. Apart from the classical vibratory fork that vibrates at only one frequency, there is a quantitative vibratory fork, Rydel-Seiffer tuning fork, which uses special extensions to adjust the frequency from 64 Hz to 128 Hz [2, 3, and 4]. Both types of vibratory forks provide only subjective information about the sense of vibration so it is not possible to perform longitudinal monitoring of changes of the sense of vibration. The sense of vibration is also tested using quantitative sensory testing (QST). The technique is based on the examination of the sense of vibration and heat on the skin, however, it depends on the cooperation and the subjective assessment of examinee and there is no uniform interpretation of obtained results among research groups [5, 6, and 7]. Aforementioned methods have unstandardised parameters of examination and depend on the active cooperation and the subjective assessment of examinee so it is necessary to standardise the method for examining the sense of vibration to obtain quantitative information suitable for further analysis.

In addition, aforementioned methods do not provide information about the functional integrity of the whole vibratory sensory pathway. The application of vibratory stimulators, used in neurophysiological testing, was therefore introduced [8]. Neurophysiological testing is based on recording the electrical activity of the brain, which can be spontaneous (electroencephalogram – EEG) or it can reflect a response to a certain stimulus (evoked potentials). The evoked potentials method has a broad applicability in medicine and in various scientific fields. It is used to assess somatosensory and motor pathways as well as higher cognitive functions. The method itself is completely noninvasive and is independent of educational and cultural influences [9].

The research performed using vibratory stimulators utilised various parameters of stimuli (stimulus duration, stimulus frequency, site of stimulation). Stimulating the muscles of forearm using stimuli of different frequencies (40 Hz, 80 Hz, 160 Hz), Münte evoked the first component 50 ms after the start of the stimulus [10]. Hämäläinen et al. investigated the stimulation of middle finger using pulses with low (24 Hz) and high (240 Hz) frequency and also registered the first evoked response as a positive peak emerging 45 ms after the start of the stimulus, with the activity localised in the contralateral primary sensory cortex [11].

In order to reach diagnosis in many systematic and neurological disorders, it is important to examine the functional integrity of the whole vibratory sensory pathway, from sensors in the skin, mechanoreceptors, up to sensory cortical regions, where information about peripheral and early cortical components is especially important. Research conducted so far resulted principally in later cortical components (around 50 ms); however, none of the studies provided information about peripheral and early cortical components.

Somatosensory evoked potentials are evoked potentials elicited using electrical stimuli, which excite sensory pathways that are anatomically almost identical to vibratory sensory pathways. They are used in everyday clinical practice and they show clearly recognisable peripheral and early cortical components. Therefore, there is a question why vibratory evoked potentials are unable to register peripheral and early cortical components and trace the activity along the whole vibratory sensory pathway.

The evoked potentials method is based on the fact that the average value of electrical activity of the brain that is elicited by repetitive stimuli is equal to the activity that emerges as a response to a single stimulus, but only if all stimuli are identical (by ignoring the influence of noise). Knowing the fact that vibratory receptors generate action potentials that are synchronous to the vibratory stimulation, it is doubtful why the induced activity cannot be registered along the whole sensory pathway, as it is the case with somatosensory evoked potentials, where even the earliest components can be easily and uniquely registered. Moreover, the response of mechanoreceptors responsible for the sense of vibration depends on the parameters of stimulation and the same stimulus should generate the same evoked response [12, 13]. All mentioned leads to the conclusion that the problem of registering the activity elicited by the vibratory stimulation along the whole vibratory sensory pathway occurs because repetitive vibratory stimuli do not have the same characteristics, which causes the inadaquate activation of vibratory receptors and the generation of action potentials with different characteristics. The inadequate activation of receptors causes asynchronous propagation of action potentials through the system and prevents the measurement of peripheral components and early cortical components of response. A late cortical response is actually the result of late cortical integration of information arriving asynchronously to the primary sensory cortex.

Vibratory stimulators which are primarily in usage have the constant amplitude of vibratory stimulus. This amplitude presents the amount of energy that is delivered to the tissue through the vibratory stimulus [8], but this is not an adequate measure since the geometrical relationship between the vibratory applicator and the tissue (examinee) is not constant. Due to this fact, even though the same amount of energy is delivered each time, the energy is not delivered entirely to the tissue and the amount of delivered energy depends on a mutual relationship between the applicator and the tissue. This causes the change in parameters between successive stimuli, and, because of the absence of identical stimuli, the unique evoked response cannot evolve. A Pacinian corpuscle, a mechanoreceptor sensitive to a vibratory stimulus, reacts to the component of pressure and is it necessary to construct a vibratory stimulator that enables the generation of successive vibratory stimuli with equal pressure characteristics of vibratory applicator.

Therefore, at the Faculty of Electrical Engineering and Computing of the University of Zagreb the vibratory stimulator was constructed, as shown in Figure 1. The main characteristic of the stimulator is maintaining the same pressure characteristics of vibratory applicator, instead of the constant amplitude of vibratory stimulus. This enables the generation of identical stimuli, with well-defined parameters, which can induce the appropriate evoked response of vibratory sensory pathway. The vibratory stimulator has very precisely defined parameters of stimuli. It is possible to choose between two waveforms

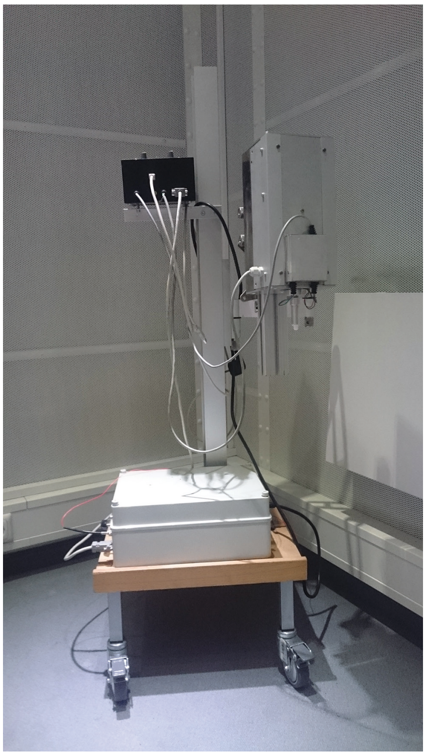

Fig. 1: Vibratory stimulator

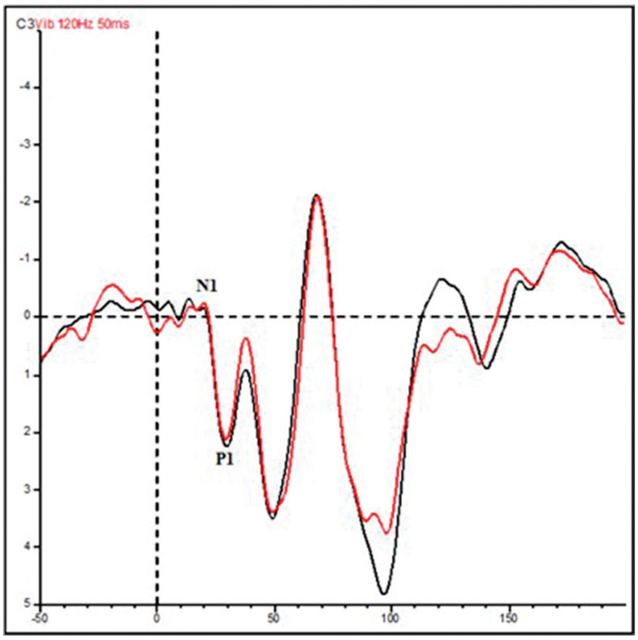

Fig. 2: Vibratory evoked potentials induced by stimulating a right hand with a vibratory stimulus

(sinusoidal and triangular), to choose the frequency in the range between 30 and 300 Hz, to choose the duration of stimulus from 10 ms to 500 ms and to choose different amplitude/intensity of pressure.

Measurements performed using the newly constructed vibratory stimulator in the Laboratory for Cognitive and Experimental Neurophysiology, the Department of Neurology, the University Hospital Centre Zagreb, have shown that for obtaining the reliable and repeatable response, which is shown in Figure 2, the stimulus with the following characteristics is necessary:

Stimulation frequency: 120 Hz

The electrical activity of the brain elicited by the vibratory stimulus with the frequency of 120 Hz shows the most resembling features as the already well known electrical activity of the brain elicited by electrical stimulation. The evoked response is composed of early components (N1, P1) and a late cortical component. When stimulating with the frequency of 120 Hz, several mechanoreceptors are active, mostly Pacinian corpuscles, with a contribution from Meissner's corpuscles, making the response to this frequency very pronounced, with the highest amplitude and with clearly distinguishable main components, and also the chosen frequency is in accordance with the available literature [14].

Stimulus duration: 50 ms

Comparing Figures 3.a and 3.b it can be seen that vibratory stimuli with the duration of 10 ms and 50 ms induce the main components of response with approximately the same latencies, so it is necessary to determine which of those durations results in a more sizeable response. It can be seen

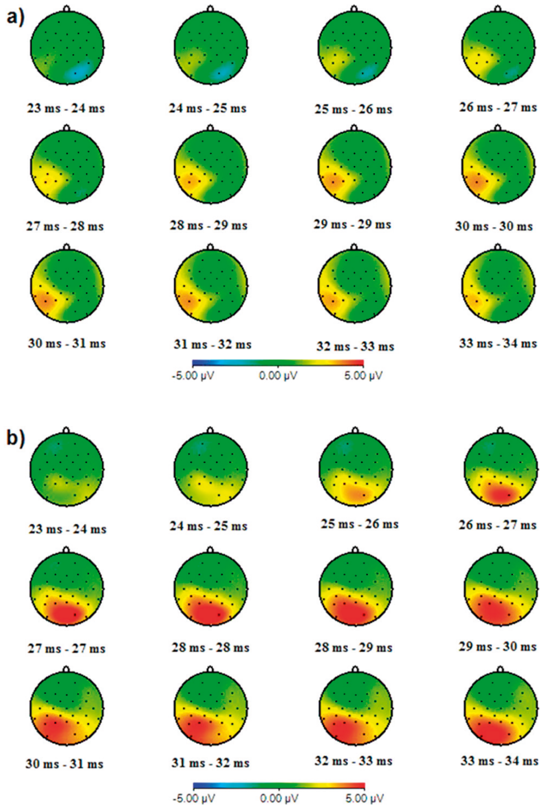

Fig. 3: Vibratory evoked potentials induced by vibratory stimulus with duration: a) 10 ms and b) 50 ms

that the vibratory stimulus with the duration of 50 ms induces the response of higher intensity, making the duration of 50 ms more eligible for further examination. The longer duration of stimulus ensures the longer exposure of the primary sensory cortex to information about the sense of vibration, which results in the stronger activation of the sensory cortex and in the stronger intensity of induced activity.

Site of stimulation: wrist

A hand has a broad representation in the somatotopic organization and a strong lateralization in the sensory region of the cortex. Wrist stimulation ensures a large enough stimulation area to activate the suitable number of Pacinian corpuscles, which have a small spatial density.

The evoked response induced by stimuli with aforementioned parameters can be uniquely registered using surface electrodes positioned above the appropriate sensory cortex. This confirms the efficiency of vibratory stimulation in the activation of vibratory sensory pathway for a particular hand and the capability of observing the functionality of vibratory sensory pathway using the evoked potentials method, which provides us with a noninvasive and quantitative insight, because the results of evoked potentials method are presented uniquely with measured values (latency, amplitude).

The existence of uniquely measured values of evoked response allows the quantitative longitudinal monitoring of examinee and also the comparison between different examinees, which was not possible so far due to lack of clearly defined and quantified early parameters of evoked response.

The presented method of vibratory stimulation is in the process of implementation into the everyday clinical practice, where it will contribute to the timely discovery and to monitoring the course of different neurological disorders.

References:

[1] M. Krbot, A. B. Sefer, M. Cifrek, Z. Mitrovic, I. Krois, and V. Isgum, "Somatosensory Vibratory Evoked Potentials: Stimulation Parameters", *Automatika*, vol. 52, no. 1, pp. 31–38, 2011.

[2] I. S. J. Martina, R. van Koningsveld, P. I. M. Schmitz, F. G. A. van der Meché, and P. A. van Doorn, "Measuring vibration threshold with a graduated tuning fork in normal aging and in patients with polyneuropathy", *J. Neurol. Neurosurg. Psychiatry*, vol. 65, pp. 743–747, 1998.

[3] S. Lai, U. Ahmed, A. Bollineni, R. Lewis, and S. Ramchandren, "Diagnostic accuracy of qualitative versus quantitative tuning forks: outcome measure for neuropathy", *J. Clin. Neuromuscul. Dis.*, vol.15, no. 3, pp. 96-101, 2014.

[4] A. Pestronk, J. Florence, T. Levine, M. T. Al-Lozi, G. Lopate, T. Miller, I. Ramneantu, W. Waheed, and M. Stambuk, "Sensory exam with a quantitative tuning fork: rapid, sensitive and predictive of SNAP amplitude", *Neurology*, vol. 62, no. 3, pp. 461-4, 2004.

[5] R. Zaslansky, and D. Yarnitsky, "Clinical applications of quantitative sensory testing (QST)", *J. Neurol. Sci.*, vol. 153, no. 2, pp. 215-238, 1998.

[6] P. S. T. Chong, and D. P. Cros, "Technology literature review: quantitative sensory testing", *Muscle Nerve*, vol. 29, no. 5, pp. 734-47, 2004.

[7] P. Siao, and D. P. Cros, "Quantitative sensory testing", *Phys. Med. Rehabil. Clin. N. Am.*, vol. 14, no. 2, pp. 261-286, 2003.

[8] J. M. Goldber, and U. Lindblom, "Standardised method of determining vibratory perception thresholds for diagnosis and screening in neurological investigation", *J. Neurol. Neurosurg. Psychiatry*, vol. 42, no. 9, pp. 793-803, 1979.

[9] C. L. Lai, R. T. Lin, L. M. Liou, and C. K. Liu, "The role of event-related potentials in cognitive decline in Alzheimer's disease", *Clin. Neurophysiol.*, vol. 121, no. 2, pp. 194-199, 2010.

[10] E. F. Münte et all., "Human evoked potentials to long duration vibratory stimuli: role of muscle afferents", *Neurosci. Lett.*, vol. 216, no. 3, pp. 163-166, 1996.

[11] H. Hämäläinen, J. Kekoni, M. Sams, K. Reinikainen, and R. Näätänen, "Human somatosensory evoked potentials to mechanical pulses and vibration: contributions of SI and SII somatosensory cortices to P50 and P100 components", *Electroencephalogr. Clin. Neurophysiol.*, vol. 75, no. 2, pp. 13-21, 1990.

[12] F. Rugiero, L. J. Drew, and J. N. Wood, "Kinetic properties of mechanically activated currents in spinal sensory neurons", *J. Physiol.*, vol. 588 (Pt 2), pp. 301-314, 2010.

[13] W. R. Loewenstein, and R. Skalak, "Mechanical transmission in a Pacinian corpuscle. An analysis and a theory" *J. Physiol.*, vol. 182, no. 2, pp. 346-378, 1996.

[14] L. Fattorini, A. Ferraresi, A. Rodio, G. B. Azzena, and G. M. Filippi, "Motor performance changes induced by muscle vibration", *Eur. J. of Appl. Physiol.*, vol. 98, no. 1, pp. 79-87, 2006.

Marina Paprika

THE IMPORTANCE OF STIMULI AND PARADIGMS IN AUDITORY EVOKED POTENTIALS

University of Zagreb, Faculty of Electrical Engineering and Computing

Auditory evoked potentials are generated by the response of the ear, the brainstem and the auditory cortex on the sound stimulus. Their application is great: from hearing screening in newborns, hearing tests, psychological research, research of the speech and language impairments, to the applications in cognitive tests of various neurological disorders.

Recording auditory evoked potentials is the similar as in the other evoked potentials. Participant sits comfortably in a chair, EEG data are collected by electrode cap on his head and he listens to stimuli presented binaurally through the in-ear headphones and distributed in the specific intervals, i.e. paradigm (Figure 1.). During stimulation, subject actively listens to stimuli or ignores them by watching the visual content. Young children, who sleep, and people in a state of coma also respond to stimulation, although they don't participate conscious in a study. EEG epochs are averaged after recording to obtain the required potentials.

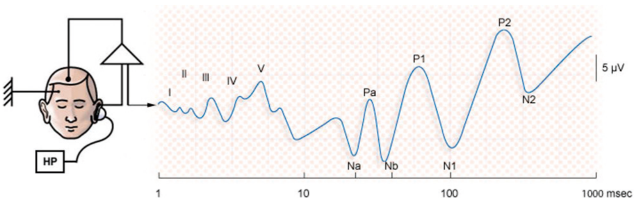

Fig. 1: The system for recording auditory evoked potentials [1]

Depending on the location of the electrical activity generation, evoked potentials are divided into the early (1 to 10 ms), middle (10 to 50 ms) and long (after 50 ms) latency evoked potentials (Figure 2.).

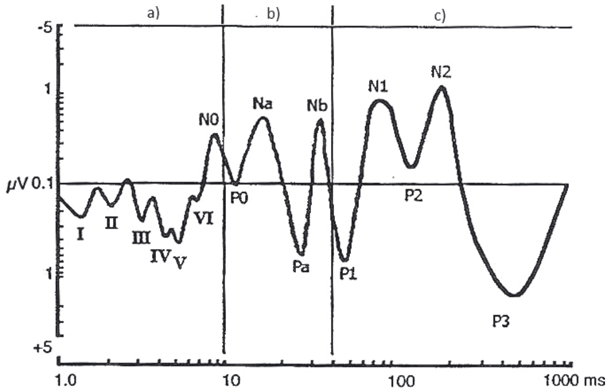

Fig. 2: Auditory evoked potentials: a) brainstem evoked potentials; b) middle latency evoked potentials; c) cognitive evoked potentials [2]

Early latency auditory evoked potentials are generated by the transmission of electrical signal on the auditory pathway to the thalamus, while middle latency evoked potentials represent thalamus electrical activity and arrival of auditory information in primary auditory cortex [2]. Long latency evoked potentials are function of cognitive factors such as attention, memory, language, etc.

EARLY LATENCY AUDITORY EVOKED POTENTIALS

Within 10 ms after stimulus occur responses of the cochlea, auditory nerves and brainstem (Figure 3.). Each of six waves (I-VI) is anatomically connected with neural structures of the auditory pathway. Diagnostic significant are latencies of the waves and latencies between the first, third and fifth wave, because these waves are most evident during the measuring. Brainstem potentials provide important information about the sound content processing at a very low level, especially in infants and young children, because early intensive rehabilitation begins with early detection of the hearing impairment.

The most used are click and sinusoidal stimuli of different frequencies and envelopes. Click stimuli are generated by the activation of a sound transducer with monophasic rectangular electric pulse of shot time (e.g. 100 μs) and presents a series of sound waves lasting a few milliseconds in frequency range 50-3000 Hz. Polarity of evoked activity depends on the polarity of rectangular pulse that affects the initial direction of the membrane acoustic transducer movement. Applying alternating stimuli eliminates this dependency.

Pure sinusoidal tones are used in finding hearing thresholds, as well as recording cognitive evoked potentials. The shape of the stimulus is determined by the maximum intensity, rise time, duration and fall time of trapezoidal envelope of the sine signal, and times are in the order of tens of milliseconds [4].

In each research, it is strived to better recording the brain activity. Due to specific structure of the cochlea and the distribution of receptors in frequency bands, we can adjust the sound stimulus in order to obtain a higher amplitude response. During the click stimulation there are no all receptors activate at the same time, different receptors, depending of the frequency, react in different time (Figure 4.).

Replies to click stimuli for higher frequencies are delayed and therefore the sum of these amplitudes is less.

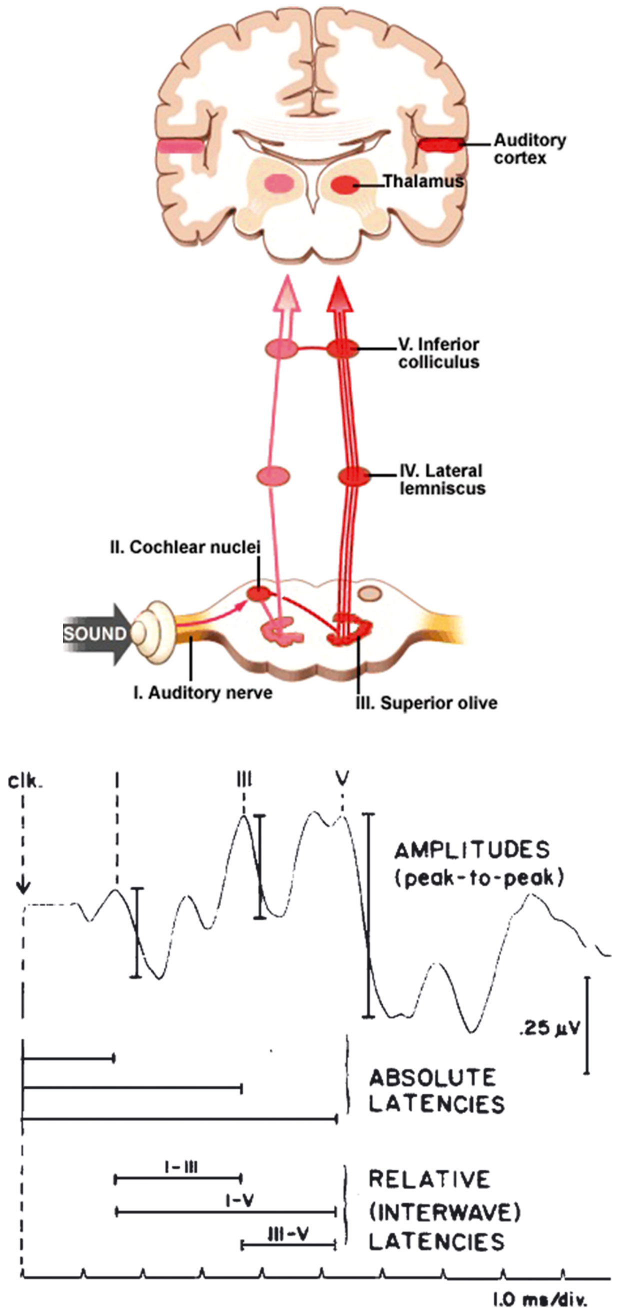

Fig. 3: Auditory pathway [1] and early latency auditory evoked potentials [3]

If the sound signal is adjusted so that its high frequency components are delayed, and all the stimuli are received at the same time to corresponding receptors, the sum of responses will be greater and we get a better signal (Figure 4.), and therefore we can get the accurate diagnoses. Such a stimulus is called a chirp stimulus [5].

Auditory brainstem response (ABR) is commonly used in paediatric diagnosis, especially in neurology and audiometry tests with the purpose to detect the hearing disorders.

ABR represents the objective audiogram (Figure 5.), and therefore provides better diagnostic information in patients whose subjective responses are unreliable. In addition to the time domain, as shown in ABR, functional testing of hearing times can be analysed in the frequency domain.

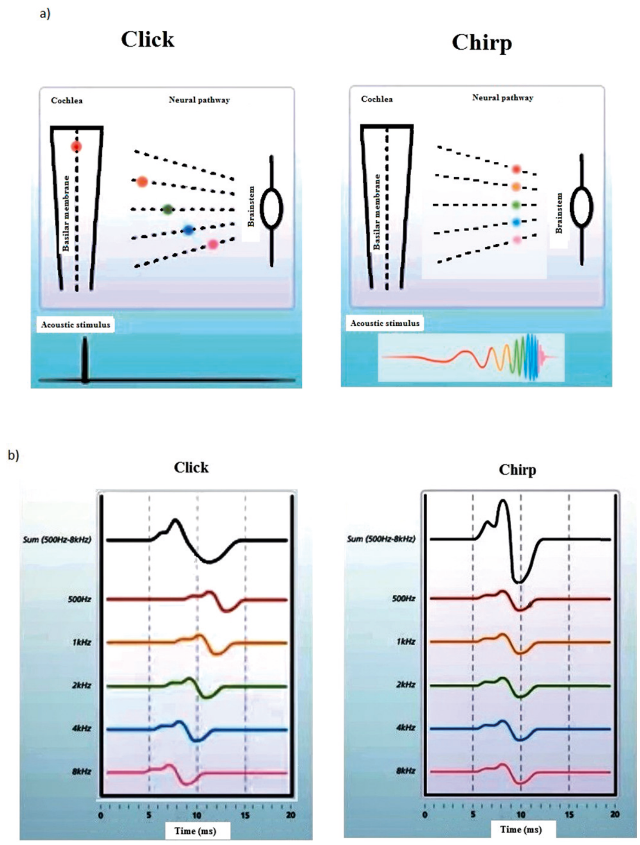

Fig. 4: a) the impact of the cochlea sound stimulation in the time; b) brainstem responses depending on the frequency components of the sound stimulus (adapted from [5])

Search based on different analysis calls Auditory Steady State Response, ASSR. The stimulus is the frequency and/or amplitude-modulated tone of 500 Hz, 1 kHz, 2 kHz and 4 kHz or broadband signals (click noise, AM noise and chirp). If there is a response, EEG activity will be synchronized with the frequency content of stimulation [6]. Due to the rapid response and to get a short time of measurement, ASSR are used in the hearing screening of new-borns.

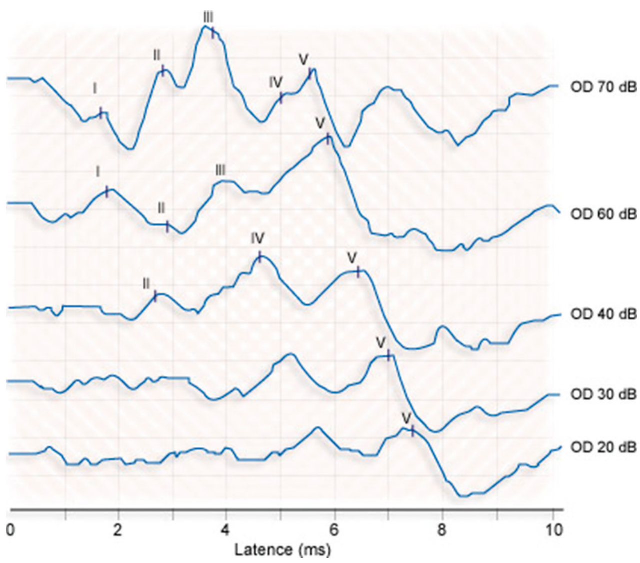

Fig. 5: ABR dependent of the auditory stimulus intensity [1]

Early latency auditory evoked potentials are unambiguous in most subjects and are thus applicable for clinical purposes. In contrast, long latency auditory evoked potentials are not represented in the diagnostic practice. There are many paradigms and stimuli used by researchers, but clinical applications are less successful for the following reasons: paradigms are complicated to use and time-demanding, relationship of the evoked components and cognitive difficulties is poorly defined, differences between the control group and the population with cognitive disabilities are not significant, and it all reduces the diagnostic value of cognitive potential [7].

LONG LATENCY AUDITORY POTENTIALS

The first responses in the auditory cortex, between 60 and 250 ms after stimulus, represent P1 and N1 waves (Figure 2.). They reflect the analysis of the physical characteristics of stimuli, e.g. intensity, frequency, pitch and timbre, and are specially influenced by attention [2]. Repeated stimuli evoke a basic N2 wave. Small probability of these stimuli contributes to increasing the amplitude of this wave, and it is considered that a component N2 corresponds to the process of categorizing stimuli [8].

When the current excitation content of the memory model is preserved, because stimuli did not cause a change in the perception, we will record only the sensory evoked potentials (N1, P2, and N2). In the process of stimulation are involved different auditory stimuli, we want to participant pays attention to some of them and therefore they are called the target, others are standard stimuli. When we insert an unknown stimulus i.e. the target stimulus, observation processes manage a changing or upgrading representations of stimuli followed the appearance of the wave P3 or P300.

A paradigm in which only the target stimulus occurs randomly in time provides a basic P3 component, as well as oddball paradigm in which between the standard stimuli are inserted target stimuli. Paradigm with three different stimuli evokes P3 wave subcomponents (Figure 6.). Subcomponents P3b, parietal maximum, occurs when between the standard stimuli is insert the target with an aim to check the subject's ability to compare and discrimination two stimuli. While the subcomponent P3a, frontal maximum, is got with one more inserted stimulus used for distraction [9]. It is considered that P3b reflects cognitive processing of stimuli [10].

When creating a paradigm, determined parameters are very important because they affect the response. Small target stimulus probability contributes to greater P3 wave amplitude and the weight of the task changes the amplitude of the wave. If the task is heavy, subject invests more effort and the amplitude is higher, which leads to the conclusion that the P3 wave generation is in relation to the amount of the effort. But if the task is too heavy and the participant is not sure whether the default stimulus is target or non-target, the amplitude decreases. It is therefore very important to work out the details of the test.

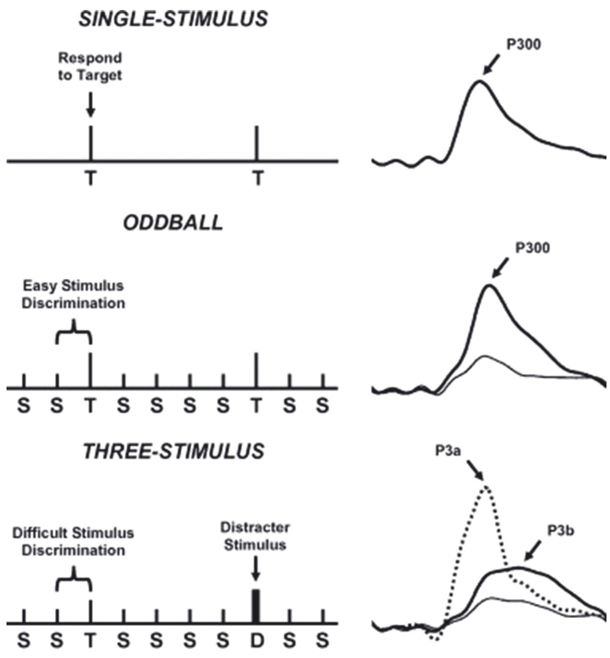

Fig. 6: Paradigms for eliciting P3 wave and subcomponents P3a and P3b [9]

Peak of the P3 wave is largest in the time range from 250 to 500 ms. For simplicity, the widely used is the oddball paradigm. Auditory oddball paradigm requires a set of standard (around 80%) tones (e.g. 65 dBHL, 1000 Hz, 50 ms duration, 10 ms fall/rise time) with randomly presented rare tones (around 20%, e.g. 65 dBHL, 2000 Hz, 50 ms duration, 10 ms fall/rise time). The interstimulus interval is about 1500 ms and it is minimum necessary 50 target stimuli. Participant counts standard tones or presses the button in the dominant hand for each target tone, thus provides the subject's attention. Very important variable is the age (latencies increase with age) and the results should be compared with the corresponding control group [11].

If the oddball paradigm is applied with the same stimuli, but the participant have to ignore the auditory stimulation and pay attention to the visual content (e.g. a silent movie or read the book), it will appear evoked potential mismatch negativity, MMN (Figure 7.).

Negative falling wave MMN, the largest on the central electrodes with the peak between 160 and 220 ms, is generated through the process of a mismatch between rare stimuli sensory inputs and sensory-memory trace that represents the physical property of the standard stimulus [8]. This process, as well as the sensory analysis of the auditory input and their coding into the memory trace, happens automatically, because MMN is elicited by changing auditory stimuli without participant's attention. MMN is especially interesting, because it is possible to access to the discrimination abilities of individuals whose sound capacities difficult to determine, including infants, young children and people with stronger cognitive impairments [7].

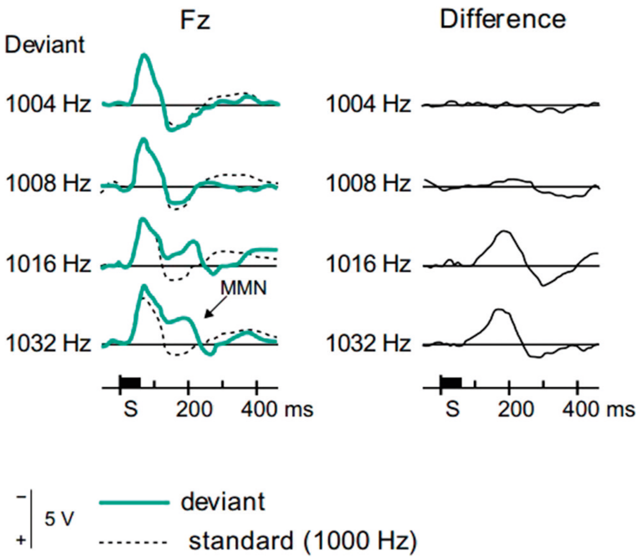

Fig. 7: MMN as a function of frequency change [11]

Only the stimulus alone does not always serve as the standard comparison for the characteristics of the stimulus. In the simplest auditory oddball paradigm the process also include factors of the larger context of the sound sequence. The basis of the appearance of MMN is extraction of the irregularity. Also, only the ratio of deviant and standard stimuli evokes no MMN, and probability alone is not sufficient for eliciting MMN (Figure 8.). The key influence on the occurrence of MMN has a repeated standard pattern. MMN is a result of a series of processes that precede the detection of differences and are sensitive to a larger auditory context [12].

MMN is counted by subtracting the averaged ERP response to the standard stimuli from the averaged response to the deviant stimuli. The interstimulus interval is about 500 ms to 1s [13], and it should be present at least 150 deviant stimuli. MMN is elicited by the different paradigms: standard oddball paradigm, the multiple deviant paradigm, paradigm without standard stimuli, uninterrupted sound paradigm.

Stimuli can also be words or sentences, and a language processing occurs after 400 ms. N400 is a negative wave maximal at the central and parietal electrodes and modulated with an expectation or anticipation words from the sentence context, a violation of semantic form is achieved by changing the last word in a sentence, a pair of words (which are more or less semantically dependent), only one

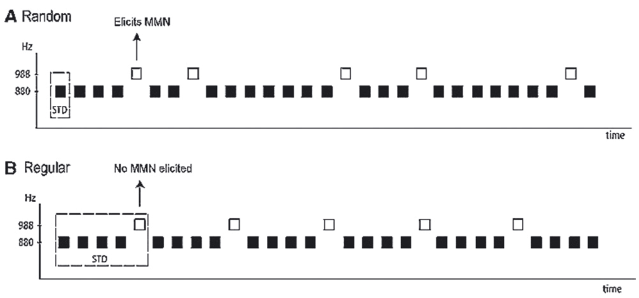

Fig. 8: A) MMN is elicited by paradigm - probability of deviant stimuli is variable; B) The regular sequence of stimuli elicit no MMN [12]

word (which participant has not heard or has rarely heard) or the images that represent an object or action [14]. It should be present at least 50 rare stimuli, also each target stimulus should be different because repetition reduces the amplitude of the wave N400, also distractor stimulus should be in the category of the same semantic field, the same frequency of occurrence in speech and the same length [7]. Late component which is correlated with a syntax process is represented by the central parietal positivity with latency 600-1000 ms. This is the wave P600 [14].

In view of the above, the cognitive evoked potentials research requires a good knowledge of paradigm development and influence of its parameters in the desired response. The same paradigm with the subject's attention or inattention can cause a variety of responses. There are many other parameters that may change the response like characteristics of the stimulus, interstimulus interval length, deviant stimulus probability, and the analysis, which can provide a clearer result if e.g. instead of in the time domain, responses are analysed in the time-frequency domain. For this reason, the auditory late latency evoked potentials still apply in the research purposes, in order to get future diagnostic value.

References:

[1] http://www.cochlea.eu/en/audiometry/objective-methods/voies-et-centres (12.02.2017.)

[2] A. Zani, A. Proverbio, The Cognitive Electrophysiology of Mind and Brain. London, UK: Academic Press, 2003

[3] http://www.asha.org/policy/RP1987-00024/ (13.02.2017.)

[4] V. Išgum, Elektrofiziološke metode u medicinskim istraživanjima. Zagreb, HR: Medicinska naklada, 2004

[5] http://www.interacoustics-us.com/technologies/ce-chirp (12.02.2017)

[6] http://www.hearingreview.com/2007/11/auditory-steady-state-response-assr-a-beginners-guide/ (13.02.2017.)

[7] H. J. Heinze, T. F. Munte, M. Kutas, S. R. Butler, R. Naatanen, M. R. Nuwer, D.S. Goodin, ''Cognitive event-related potentials'', International Federation of Clinical Neurophysiology, pp. 91-95, 1999

[8] S.J. Luck, An introduction to the event-related potential technique. Cambridge, MA: The MIT Press, 2005

[9] J. Polich, ''Updating P300: An integrative theory of P3a and P3b'', Clinical Neurophysiology. vol. 118, pp. 2128-2148, 2007

[10] C.A.Nelson, M. Luciana, Handbook of Developmental Cognitive Neuroscience. London, UK: The MIT Press, 2001

[11] C. Duncan a, R. Barry, J. Connolly, C. Fischer, P. Michie, R. Näätänen, J. Polich, I. Reinvang, C. Van Petten,“ Event-related potentials in clinical research: Guidelines for eliciting, recording and quantifying mismatch negativity, P300 and N400“, Clinical Neurophysiology, vol. 120, pp. 1883–1908, 2009

[12] E.S.Sussman, S. Chen, J. Sussman-Fort, E. Dinces,“ The five myths of MMN: Redefining how to use MMN in basic and clinical research“, Brain Topography, pp. 553-564, 2014

[13] C. Duncan a, R. Barry, J. Connolly, C. Fischer, P. Michie, R. Näätänen, J. Polich, I. Reinvang, C. Van Petten,“ Event-related potentials in clinical research: Guidelines for eliciting, recording and quantifying mismatch negativity, P300 and N400“, Clinical Neurophysiology, vol. 120, pp. 1883–1908, 2009

[14] A.D. Friederici, I. Wartenburger, ''Language and brain'', WIREs Cognitive Science, vol. 1, pp. 150-159, 2010

HATZ News

CURRENT AND FORTHCOMING ACTIVITIES OF THE CROATIAN ACADEMY OF ENGINEERING IN 2017

In accordance with its accepted Program of Work and Activities in 2017, the Croatian Academy of Engineering continues with intensive activities, especially concerning auspices of conferences and meetings, the organisation of its own conferences and co-organisation of conferences with other prominent academies, scientific organisations, and companies in Croatia and abroad. The Academy also participates regularly in the meetings and conferences of public interest, organised by other related institutions.

Auspices of the Academy

- Faculty of Textile Technology in Zagreb – ***10th Scientific and Professional Colloquium TEXTILE TECHNOLOGY AND THE ECONOMY – „Complementarity of Science, Technology, and Design“***, Zagreb, January 24, 2017
- Josip Juraj Strossmayer University of Osijek, Faculty of Food Technology and Biotechnology in Osijek, Faculty of Agriculture in Osijek, Faculty of Civil Engineering in Osijek, Department of Biology of the J.J. Strossmayer University of Osijek, Department of Chemistry of the J. J. Strossmayer University of Osijek, Faculty of Food Technology and Biotechnology of the University of Zagreb, European Hygienic Engineering and Design Group (EHEDG), DANUBEPARKS – Network of Protected Areas along the Danube River, Croatian Food Agency, Croatian Agency for the Environment and Nature, Hrvatske vode – VGO Osijek, Osijek-Baranja County, Vodovod-Osijek, Ltd., Public Institution Kopački Rit Nature Park, Institute of Public Health of the Osijek-Baranja County – ***7th International Conference „Water for All“***, Osijek, March 9-10, 2017
- Croatian Colour Society (HUBO) – ***International Colour Day 2017 (MDB 2017)***, Zagreb, March 21, 2017
- Croatian Chamber of Mechanical Engineers – ***5th International Congress MECHANICAL ENGINEERS' DAYS***, Vodice, March 29-31, 2017
- Faculty of Transport and Traffic Sciences in Zagreb – Department of Water Transport, University of Zagreb - ***Round Table Discussion "The Future of Maritime Line Passenger Transport in the Republic of Croatia"***, Borongaj Scientific and College Campus, Zagreb, April 5, 2017
- Faculty of Mechanical Engineering and Naval Architecture in Zagreb, University North in Varaždin, Croatian PLM Association – ***International Scientific Conference MOTSP 2017 „Management of Technology – Step to Sustainable Production“***, Dubrovnik, April 5-7, 2017
- Croatian Society for Biotechnology (HDB), European Biotechnology Thematic Network Association (EBTNA), EUROBIOTECH, and University of Zagreb – Faculty of Food Technology and Biotechnology - ***European Biotechnology Congress 2017***, Dubrovnik, May 25-27, 2017
- Faculty of Transport and Traffic Sciences of the University of Zagreb, Croatia and Faculty of Logistics of the University of Maribor, Slovenia - ***International Conference on Traffic Development, Logistics & Sustainable Transport (ZIRP 2017) – "New Solutions and Innovations in Logistics and Transportation"***, Opatija, June 1-2, 2017
- Croatian Cartographic Society (HKD) – ***13th Colloquium „Geo-heritage, Geo-information, and Cartography“***, Selce, September 7-9, 2017
- Faculty of Electrical Engineering in Osijek – ***International Conference on Smart Systems and Technologies 2017 (SST 2017***), Osijek, October 11-13, 2017

(Co-)organisation of the Academy's Conferences and Meetings

- ***8th Joint Session of the Council and Co-ordination of the Croatian Academy of Medical Sciences, Croatian Academy of Engineering, Croatian Academy of Legal Sciences, and Academy of Forestry Sciences***, Zagreb, January 30, 2017
- Croatian Academy of Engineering – Department of Chemical Engineering and Centre for Environmental Protection and Development of Sustainable Technologies, PLIVA Croatia, Inc., and Model, Ltd. – ***Scientific and Professional Conference „Mathematical Modelling and Numerical Simulations' Application in the Chemical Process Industry“***, Zagreb, February 23, 2017
- Croatian Engineering Association, Croatian Academy of Engineering, and Faculty of Forestry in Zagreb – ***3rd Croatian Engineers' Day***, Zagreb, March 2, 2017
- Croatian Academy of Medical Sciences, Croatian Academy of Engineering, Croatian Academy of Legal Sciences, and Academy of Forestry Sciences – Scientific Symposium ***„Modern Technologies: The Ethics of Utilisation and the Legal Regulations“***, Zagreb, March 17, 2017
- Croatian Academy of Engineering, Public Open University Zagreb, and Faculty of Mechanical Engineering and Naval Architecture in Zagreb – ***Round Table Discussion „Teachers' Competences in the Higher Education“*** *and Presentation of the book „The Curricular and Didactic-methodical Grounds of the Higher Education Teaching“ (authors: Duško Petričević, PhD, Prof. Gojko Nikolić, PhD, Daniel Domović, BSc Comp, and Jelena Obad, BSc Psych)*, Zagreb, March 28, 2017
- Croatian Academy of Engineering – Department of Graphical Engineering and Centre for Graphical Engineering, and Školska knjiga Zagreb, Inc. **– *International Scientific Conference „Printing & Design 2017“***, Zagreb, March 9, 2017
- Croatian Academy of Engineering and Faculty of Electrical Engineering and Computing in Zagreb – ***Round Table Discussion „Status and Future of Technological and Biotechnological Sciences in Croatia in the 21st Century“***; *Presentation of the "Annual 2016 of the Croatian Academy of Engineering" (in Croatian), and Presentation of the New Issues of HATZ Bulletins in Croatian („Tehničke znanosti"), and in English („Engineering Power")*, Zagreb, May 8, 2017
- Croatian Academy of Engineering and University of Zagreb – ***32nd Annual (Elective) Assembly of the Croatian Academy of Engineering***, Zagreb, May 15, 2017

- Croatian Academy of Engineering – ***Round Table Discussion „The Know-how Required for Successful Conception of and Decision-making on the Implementation of Major Energy Projects in the Republic of Croatia“***, Zagreb, October/November 2017
- Polish Academy of Sciences (PAN) and European Council of Academies of Applied Sciences, Technologies, and Engineering (Euro-CASE) – ***Euro-CASE Annual Conference 2017 „Cybersecurity“***, Poznań, Poland, November7-8, 2017
- Real Academia de Ingeniería (RAI), Spain – ***CAETS Convocation 2017***, Madrid, Spain, November 13-16, 2017
- National Academy of Engineering (NAE US – CAETS) and Technology Academy Finland (TAF – Euro-CASE) - ***The 2017 EU-US Frontiers of Engineering Symposium***, University of California, Davis, CA, USA, November 16-18, 2017

Participation of the Academy at the Conferences and Meetings of Public Interest

- Croatian Academy of Sciences and Arts – Scientific Council for Technological Development – ***Lecture by Academician Božidar Liščić*** *(HAZU Full Member and HATZ Emeritus)****, „How to Realise Intelligent Product Specialisation for the Export Products of High Added Value?”***, Zagreb, January 24, 2017
- Croatian Academy of Sciences and Arts – ***Opening of the 12th Night of the Musea – „Music and the Great Musicians – Their Influence on the Society“***, Zagreb, January 27, 2017
- Croatian Academy of Medical Sciences – ***Public Lecture “Trends in Pharmaceutical Industry and the Role and Position of the Generic Industry” (lecturer: Mihael Furjan, BSc (Econ)****, Pliva Croatia, Inc., President of the Management Board and CEO for Southern and Eastern Europe)*, Zagreb, January 31, 2017
- Croatian Academy of Sciences and Arts – ***Public Lecture by Marijana Borić, PhD, “Faust Vrančić – 400 Years After”*** *(on the occasion of the 400th Anniversary of Death of Faust Vrančić)*, Zagreb, February 2, 2017
- Croatian Engineering Association (HIS), Faculty of Forestry in Zagreb, and Croatian Forestry Society – ***Round Table Discussion „The Role of Wood Technology and Forestry in the Circular Economy”***, Zagreb, February 27, 2017
- Croatian Academy of Medical Sciences – ***Public Lecture “Robots in the Medicine“ (Lecturer: Prof. Gojko Nikolić, PhD),*** Zagreb, February 28, 2017
- Croatian Academy of Sciences and Arts – ***Project Presentation Ceremony: The New Passenger Terminal of the Franjo Tuđman Airport Zagreb (authors: Academician Branko Kincl, Academician Velimir Neidhardt, and the late Prof. Jure Radić, PhD)***, Zagreb, March 20, 2017
- University of Zagreb – Faculty of Mechanical Engineering and Naval Architecture – ***Round Table Discussion „Draft Amendment Proposal of the Strategy of National Security and the Long-term Plan of Development of the Croatian Navy by Means of Its Own Development by 2024“***, Zagreb, March 9, 2017
- Croatian Academy of Sciences and Arts – Department of Natural Sciences and Department of Mathematical, Physical, and Chemical Sciences – ***Meeting on the Occasion of the 160th Anniversary of Death of Academician Andrija Mohorovičić“,*** Zagreb, March 21, 2017
- Groupe interacadémique pour le développement (GID) – Euro-Mediterranean Academic Network (EMAN) – ***Forum Parmenides VIII „What Knowledge to Reconcile the Evolution of Port Facilities with Sustainable Development in the Mediterranean?“,*** Genoa, Italy, March 21-23, 2017
- Croatian Academy of Sciences and Arts and Croatian Science Foundation – ***1st Colloquium: Lecture by Academician Mladen Obad-Šćitaroci*** *(Full Member of HAZU and Member of HATZ in the Department of Architecture and Urban Planning),* ***„Cultural Heritage Advancement in the Context of the Heritage Urbanism“,*** Zagreb, March 23, 2017
- European Research Council (ERC), Ministry of Science and Education of the Republic of Croatia, Agency for Mobility and EU Programmes – ***The 10th ERC Anniversary Jubilar Conference „European Research Council – Ten Years of Excellent Ideas“***, Zagreb, March 27, 2017
- Nikola Tesla Innovation Centre (ICENT) – ***2nd Workshop within the CROBOHUB Project on Research and Development in the Field of Robotics***, Zagreb, March 27, 2017
- Croatian Academy of Medical Sciences – ***Public Lecture “Croatian Forests’ Ecosystems as the Natural Habitats of Zoonoses Causative Agents” (Lecturer: Prof. Josip Margaletić, PhD,*** *Member of Academy of Forestry Sciences),* Zagreb, March 28, 2017
- Tehnix, Ltd., and Zagreb Fair – ***2nd International Technological Conference for Sustainable Waste Management (***within the *9th International Fair of Environmental Protection and Communal Equipment – EMAT)*, Zagreb, April 5, 2017
- Croatian Academy of Sciences and Arts – ***Lecture by Guste Santini, PhD, „POSSIBLE COURSES OF TAX POLICIES CONVERGENCES WITHIN THE EU FRAMEWORK – A MESSAGE TO CROATIA“***, Zagreb, April 12, 2017
- Croatian Academy of Sciences and Arts – Scientific Council for Traffic – ***International Scientific Congress „Valorisation of Intermodal Logistical Corridor Ploče-Mostar-Sarajevo-Vukovar (Croatian Middle Adriatic-Danube Region) ”***, Zagreb, April 25, 2017

HATZ News Editor
Melanija Strika, Business Secretary of the Croatian Academy of Engineering

Engineering Power, *Bulletin of the Croatian Academy of Engineering*
Publisher: HATZ, 28 Kačić Street, P.O.Box. 59, HR-10001 Zagreb, Croatia
e-mail: HATZ@hatz.hr, web: www.hatz.hr
Vol. 12(2) 2017 – ISSN 1331-7210
Editor-in-Chief: Vladimir Andročec
Editor: Zdravko Terze
Guest Editor: Mario Cifrek
News Editor: Melanija Strika
Phone: + 385 1 4922 559
Technical Editor: Vladimir Pavlić, GRAPA, Zagreb, Croatia
Printed by: Tiskara Zelina Ltd, Zelina, Croatia